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INJURIES OF THE PARIETES AND EXTREMITIES

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MANY men have made helpful contributions toward solving the problems involved in the treatment of wounds and compound injuries. With all deference to the legion of surgeons whose efforts have culminated in the methods of treatment in use today four men should be mentioned—one no longer living—whose writings deserve careful reading by every surgeon interested in the treatment of wounds. Those men are Hugh Owen Thomas (of the Thomas splint), H. Winnett Orr, Mont Reid, and Vilray P. Blair. Their contributions, needless to say, are concerned particularly with surgical principles rather than with exact details of technique.

One of the primary principles that guided Thomas in his treatment of wounds and injuries is epitomized in his oft repeated dictum, "Inflamed and injured tissues need rest," a principle oft forgotten, but rediscovered during the past few years and emphasized so often and so forcibly that it should never again be relegated to a secondary place in surgical teaching. Orr, and subsequently Trueta, reaffirmed this principle.[1] Orr demonstrated its importance particularly in the care of patients with chronic and persistent infection of bone. He demonstrated a second principle, which his kindliness and consideration for his professional colleagues did not permit him to emphasize, namely, that nature unhindered can often accomplish more for the patient with a compound fracture or a chronic osteomyelitis than the unthinking surgeon who repeatedly tears down healing tissue and constantly adds infection to an open wound as he dresses it with careless hands, and breathes and talks over it with unmasked nose and uncovered mouth, perhaps when the very atmosphere is harboring virulent bacteria. If such a statement sounds harsh to the reader's ear he has only to read some of the comments that have come from overseas in the past 12 months to realize that much harsher things have been said.[2]

Blair's paper on the helpful effect of pressure on wound healing also represents a principle which in Homans' words has been "perennially discovered, discredited, forgotten, rediscovered and reaffirmed." In spite of the repeated emphasis of Blair and many others on the importance of pressure in preventing congestion and helping to maintain the circulation in the subcutaneous tissues, in spite of the fact that almost every layman knows that the simplest way to stop bleeding,

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[1] "In spite of Dr. Trueta's careful instructions, many surgeons seem to feel that a white crust round a dressing casts a magic spell over the wound it encloses; they will discuss the supposed action of the bacteriophage and of calcium ions in healing processes while ignoring the obvious fact that the chief purpose of a plaster cast is to confer absolute rest on an injured part, but that it can do so only if it is adequate in size, correctly designed and well applied." (Lancet, 1940, 2: 45.)

[2] "Often (hospital) infection occurs in the already infected wound. Sepsis is piled upon sepsis, etc."

whether from an open wound or from subcutaneous trauma, is by the application of moderate pressure, only after continued use had repeatedly demonstrated its value in the treatment of compound fractures of the long bones was it generally recognized that the smooth uniform pressure of a plaster cast was an important factor in preventing exudation into the injured tissues and in helping to maintain an adequate circulation. That the same pressure can be advantageously applied, whether with plaster or some other form of pressure dressing, whenever there has been an injury of the soft tissues alone, and that it is of greatest value where the injury is of great extent, as in the case of a severe burn, has often been demonstrated but too often before unseeing eyes.

Reid's paper "Some Considerations of the Problems of Wound Healing," could well be required reading for every surgeon who has the obligation and opportunity of treating patients with open wounds. It is a thoughtful, comprehensive and wholly admirable discussion of the factors at work and the principles involved in wound repair.

THE principles involved in the care of wounds of the parietes and extremities do not differ from those applicable to all wounds. Primary considerations are: (1) arrest of hemorrhage and treatment of shock; (2) prevention of additional contamination and trauma; (3) diagnosis of the extent of injury; (4) conversion of the contaminated wound into a clean wound if the time interval still permits; (5) removal of foreign material and devitalized tissue; (6) repair of injured structures; (7) purposeful dressing and splinting to provide rest and an adequate circulation for injured tissues, whether bone or soft tissues; (8) cleanly surgical care until healing is complete. Under conditions of stress and when suddenly confronted with many seriously injured patients the surgeon cannot carry out the treatment suggested in the paragraphs immediately following. In subsequent paragraphs methods of treatment to be adopted in emergencies are outlined. Unless, however, the surgeon keeps clearly in mind the basic surgical principles that underlie successful treatment he can easily fail to accomplish satisfactory results, no matter what conditions obtain.

1. ARREST OF HEMORRHAGE AND TREATMENT OF SHOCK

It is often forgotten that simple pressure will stop bleeding in the majority of cases *if the pressure is applied in the right place.* Digital pressure over a few pads of sterile gauze is more likely to be effective than a massive gauze dressing held with a circular bandage. A spurting vessel can be caught with a sterile hemostat and the forceps included in the covering dressing. The hasty effort to arrest bleeding with ungloved hands and incompletely sterilized instruments may lead to further and serious wound contamination. If a constrictor must be used the inflated blood pressure cuff is least likely to lead to compression injury of nerves and soft tissues.

"Elevation of the bleeding wound is of importance, if it can be done without too much manipulation. In our dispensary we see many people come in with bleeding wounds and improperly applied tourniquets. Removal of the tourniquet and simple elevation of the part stop the bleeding" (Reid).

The necessity for recognition and treatment of shock needs no emphasis. Many a surgeon has learned from bitter experiences the disastrous results that can follow operation on the pale, severely injured patient "with a rapid pulse and cold nose." The importance of the subject has been stressed by every writer concerned with the treatment of wounds. In the surgical emergencies of today patients with impending or actual shock should receive more skillful and efficient treatment than it has ever been possible to achieve in the past.

2. PREVENTION OF ADDITIONAL CONTAMINATION AND TRAUMA

The most feared sources of added contamination of open wounds are the uncovered noses and mouths of first aid workers and of all others who share in the subsequent care of the patient; the ungloved hands of those who are constantly working with patients with contaminated wounds; incompletely sterilized instruments and surgical supplies;

dust borne infection in wards or dressing rooms constantly used in the care of patients with infected wounds.[1] The most common forms of trauma superimposed on the initial injury are the chemical trauma of powerful antiseptics, the mechanical trauma of probing and "investigation" of the wound, and the trauma that results from constant movement of unsupported and unsplinted fractured tissues.

How can these be reduced to a minimum? First, and of very great importance, by having all personnel working with patients with open wounds capped and masked. Second, by covering the open wound at the earliest possible moment with an occlusive sterile dressing bandaged in place with moderate pressure and left undisturbed until adequate surgical care can be given and under the most favorable conditions available. Third, by avoiding the addition of tincture of iodine and other so-called antiseptics that fix, coagulate, and destroy living tissues, and that are particularly damaging to the delicate tissues underneath the skin which are ill adapted to resist such injury.[2] Fourth, by avoiding any probing or examination of the open wound. Fifth, by immobilizing the injured part as completely as possible and at the earliest possible moment by the simplest method available that provides rest for the injured tissues and uniform pressure over the affected area.

3. DIAGNOSIS OF THE EXTENT OF INJURY

It is easy to forget that diagnosis should precede treatment when one is dealing with patients with open wounds and under unusual and trying conditions. *An estimate of the patient's general condition and recognition of the presence of multiple injuries and unusual injuries are of primary importance.* The tiny wound of the buttock that marks the site of entry of a shell splinter that has perforated a viscus, the scratch of the lumbar region at the point of entry of a metal fragment that has perforated the colon, the bleeding wound of an extremity that diverts attention from a compression of the spine are only a few of the many "traps" that can be avoided by unremitting watchfulness and care.

Injuries of the extremities lend themselves particularly to diagnosis of the extent of local injury because of the signs that can usually be elicited distal to the site of injury. One must consider in turn blood vessels, bones, nerves, and tendons.

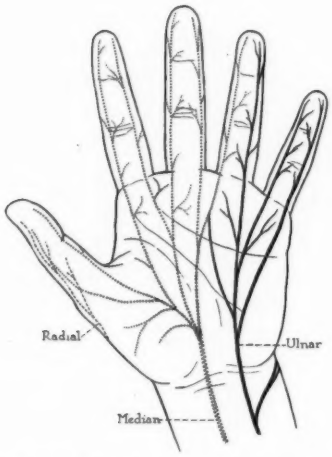
Injuries of blood vessels are evidenced by the obvious signs of hemorrhage, by the pallor or cyanosis of all the extremities when the blood escapes, and by the increasing swelling, tension, and discoloration of the affected limb that accompany concealed hemorrhage. The absence of radial or tibial pulse and the lowered temperature of the limb are significant and easily elicited signs of severe obvious or concealed vascular injury. Combined arteriovenous injuries are not uncommon as a result of deep penetrating wounds.

Injuries of bone are not likely to be overlooked because of the obvious loss of function invariably present. In cases of doubt it is wise to assume that some bone injury is present. The exact information that can be obtained from x-ray examination is often invaluable.

Injuries of nerves are usually easy to recognize and are of all injuries most often overlooked. The motor and sensory signs of median, ulnar, and radial nerve injury in the upper extremity, and of tibial and peroneal injury in the lower are clear cut, easy to elicit, and within a period of from 3 to 6 hours after injury are not misleading. Later, edema and swelling may cause pressure upon nerve fibers and give signs of division when only compression is present. In Figures 1 to 6 are indicated methods of recognizing the most common and important nerve injuries involving the upper extremities. With reference to the lower extremities it is important to remember that sensation over the anterior and lateral aspect of the leg and dorsum of the foot is controlled

[1] The admirable papers of Hare and the reports of Colebrook and Fleming have stressed the importance of human sources of contamination and the incriminating evidence yielded by repeated examination of the bacteriological flora of open wounds.

[2] "Today, with our knowledge of the delicacy of growing living cells and of their lethal susceptibility to alcohol, ether, iodine, mercurochrome, merthiolate, carbolic acid, bichloride of mercury, and countless other substances, people go blithely on pouring them into open, fresh wounds to kill living cells and to complicate the process of wound healing and to promote the chances of infection. So far as fresh traumatic wounds are concerned we would today be far better off with a total ignorance of all chemical bactericidal agents and if we only utilized our knowledge of bacteria and of wound healing by gentle mechanical cleansing of the surrounding skin and open wound of all dirt, foreign bodies, dead or devitalized tissue and by flooding the invisible bacteria away by means of sterile salt solution." (Reid, Mont R. *N. England J. M.*, 1936, 215: 753–765.)



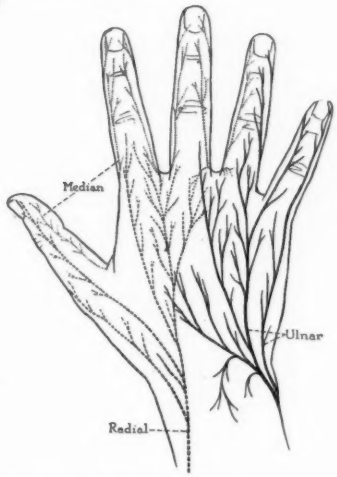


Fig. 1, left. The sensory nerve supply of the palm (after Spalteholtz).
Fig. 2. The sensory nerve supply of the dorsum of the hand (after Spalteholtz).

by the common peroneal nerve; over the medial and posterior aspect of the leg and plantar surface of the foot by the tibial nerve.

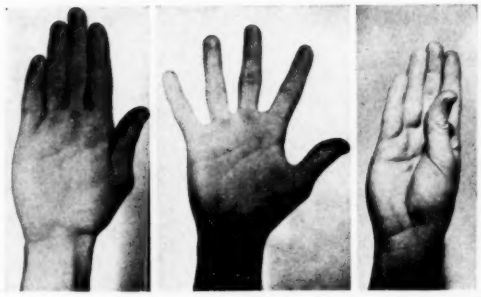
Dorsal flexion at the ankle and extension of the toes are controlled by the common peroneal; extension at the ankle joint and flexion of the toes by the tibial nerve.

Tendon injuries can be recognized as definitely as nerve injuries. The diagnosis requires a few minutes of time and accurate anatomical knowledge (Figs. 5, 6).

4. CONVERSION OF THE CONTAMINATED WOUND INTO A CLEAN WOUND

Surgeons are not all in agreement as to the best method. Theoretically, if one could cleanse the area about the wound, and carry out complete excision of contaminated tissue without permitting the knife to come in contact with the contaminated surface of the open wound, he would rid the patient of all contaminated tissue "at one stroke" (Figs. 7, 8). Practically, such a procedure is difficult to carry out even with great care and in the case of a superficial wound. It is almost impossible to accomplish in the treatment of most wounds because wound tracts are irregular, often tortuous in direction and surprisingly deep; and because one cannot sacrifice essential structures in order to accomplish complete excision of a contaminated wound. While complete excision may be applicable in the case of very superficial wounds, or wounds in which subcutaneous tissue and muscle alone are involved, the surgeon who attempts to apply the principle of complete excision to all wounds finds himself at a loss when he is confronted with tendons, nerves, blood vessels and perhaps bone fragments and open joint cavities exposed to the same contamination which he has been attempting to remove by a complete excision.

In our judgment the most certain and practical method of converting every type of contaminated wound into a clean wound is first of all to wash the area around the wound and then the wound itself thoroughly, patiently, and gently with plain white soap and water, applied with soft cotton and with hands covered with sterile gloves (Fig. 9), and secondly to irrigate the wound with sterile salt solution. While the area about the wound is cleansed the wound itself is protected with the inner portion of the occlusive dressing originally applied. When the surrounding area is cleansed the dressing is removed and the wound itself cleansed in the same way. If the



a b c

Fig. 3. a, Adduction of the fingers toward the middle finger; b, abduction of the fingers from the middle finger; and c, adduction of the thumb toward the hand are carried out by the interossei, the muscles of the hypothenar eminence and the adductor pollicis, all of which are supplied by the ulnar nerve.

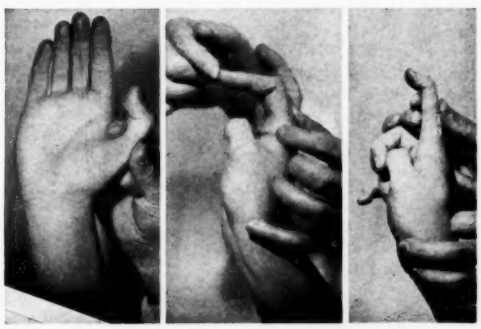
a b c

Fig. 4. a, Flexion at the metacarpophalangeal joints is produced by the lumbricals and interossei. b, c, With injury or division of the median and ulnar nerves below the middle of the forearm the power of flexion at the metacarpophalangeal joints is lost; the fingers can still be flexed at the interphalangeal joints by the long flexor tendons.

wound is clean cut, incised and with little evidence of contamination no effort is made to wash the wound surface with soapy solution, but we believe no harm is done if the solution comes in contact with it. The more jagged and irregular the wound the more careful and prolonged the cleansing; if necessary wound edges are held apart with retractors, and if indicated the cleansing solution and the gloves of the operator are changed during the cleansing procedure. Finally, every recess of the wound is thoroughly irrigated with warm sterile salt solution.

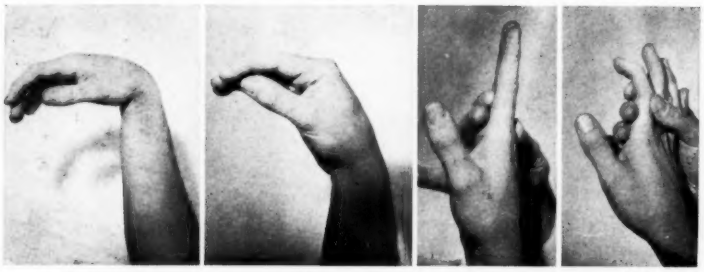
Why this particular method? Because it is simple; because it requires only patience and care, and not unusual surgical ability; because it is applicable to every type of injury; because it works.

As evidence of the successful results that can be obtained by such a method and of the fact that the theoretical danger of spreading contamination by cleansing wound surfaces is of little practical importance I would cite the following facts: Drs. Michael Mason, Harvey Allen, and I have carried out this method in the treatment of all open wounds which have come under our care during the past five years. Some of them have been extensive and comparable to the serious injuries seen in war (Figs. 10 to 12). In only 3 of 103 cases with extensive injuries in which the patient came within 2 hours of the time of injury, in which first aid care had been limited to the application of a pressure bandage and a sterile dressing, and in which the covering tissues could be approximated or completely replaced was there failure of primary union. Secondly, only since this method of treatment has been introduced at the Cook County Hospital have we consistently seen patients return to the Hand Clinic with primary healing after repair of open wounds with division of nerves and tendons. Thirdly, surgeons who are handling large numbers of cases of compound



a b c

Fig. 5. a, If the proximal phalanx of the thumb is held fixed active flexion at the interphalangeal joint is due solely to the action of the flexor pollicis longus. If the muscle or tendon is injured or divided, flexion is limited or the thumb remains fixed in extension. b, Position of the finger after division of the flexor profundus; active flexion at the proximal interphalangeal joint is produced by the flexor sublimis, but the finger remains extended at the distal interphalangeal joint. c, If the flexor profundus is intact the finger can be flexed at the distal interphalangeal joint.



a b c d

Fig. 6. a, Drop wrist of musculospiral or radial nerve injury. b, Loss of power of extension of the fingers due to injury or division of the extensor communis digitorum. c, With the proximal phalanges fixed or supported the fingers can be extended by the action of the lumbricals and interossei even though the extensor communis is divided. d, Loss of power of extension at the distal interphalangeal joint, due to division of the extensor tendon opposite the joint or avulsion of the tendon from its insertion on the distal phalanx.

injuries are obtaining similarly consistent results.

"The study of 21,862 injuries resulting in 12,044 compound wounds, revealed that hospitalization was necessary in 18 cases in which the primary care consisted of white soap and water cleansing and excision of only devitalized tissue. Seventy-five per cent of these compound injuries involved the wrist and hand. Of these 9,195 cases only 10 patients required hospitalization. Because these injuries were so uniformly contaminated and so difficult of cleansing, and further, because in no instance in which primary soap and water cleansing was given, was it necessary to hospitalize an individual for infection, we feel that this is the severest test for the efficacy of the method. It is likewise seen that it is successful in the hands of the nurses who care for the great majority of the minor compound wounds. In 101 cases of compound fractures, there were 4 infections and in no instance osteomyelitis or delayed union from infection" (Kerrigan).

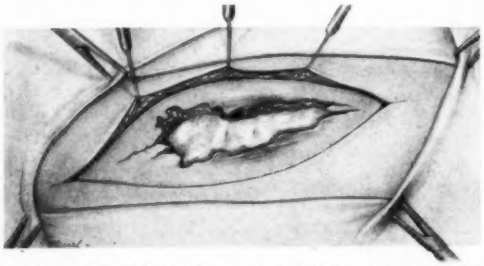


Fig. 7. The skin has been painted with a skin antiseptic up to the wound edges and draped. No skin antiseptic and no alcohol, ether, or soap has been allowed to enter the wound. The excision of the wound has been started. (Reid and Carter, *Ann. Surg.*, 1941, 114: 9.)

5. REMOVAL OF FOREIGN MATERIAL AND DEVITALIZED TISSUE

After wound cleansing is completed removal of any foreign bodies that remain and complete excision of devitalized tissue are carried out. If the contaminated wound has been transformed into a clean wound by careful cleansing the surgeon works at a great advantage. He is not tempted to sacrifice tissue ruthlessly to assure complete removal of possible contamination; and it has been our observation that the effect of irrigation on injured tissues often helps him to differentiate devitalized tissue from living tissue.

What is devitalized tissue, and how can it be recognized? Skin that is dead white, grayish-white, or purple, that does not bleed when cut nor change in color when gentle pressure is applied with a warm moist pack; muscle that is gray or reddish-gray and that does not contract when gently pinched; tendons and nerves that are discolored with blood, contused, and fragmented; bone that is detached from muscle and periosteum—all these have little or no chance of survival, furnish excellent media for bacterial growth and jeopardize wound healing.

The importance of excising completely tissue which is devitalized should not lead the surgeon into the error of sacrificing tissue which can be preserved. "It is particularly important that skin should not be sacrificed

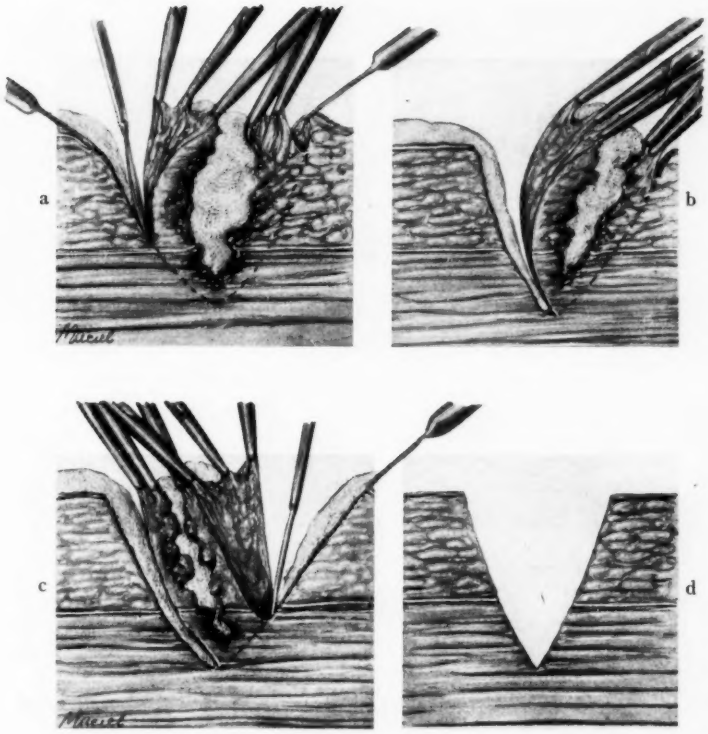


Fig. 8. a, Hemostats have been applied to the skin edge which is to be excised. The excision has been carried down to the muscle. Fresh pads moistened with saline have been advanced down the clean side of the wound as the incision is deepened. b, The excision has been completed on one side. Note the protection by the gauze pad. c, The excision has been nearly completed. d, The completed excision. The wound is now irrigated copiously with normal salt solution and fresh drapings are applied. (Reid and Carter, *Ann. Surg.*, 1941, 114: 10.)

needlessly, for of all tissues it is the most viable and most necessary" (*Lancet*, 1940, 2: 46). The needless sacrifice of bone fragments still attached to muscle and periosteum and the subsequent failure of the fractured bone to unite were often commented upon during the last war. As Mr. Anderson has emphasized, excision of devitalized tissue should begin at the proximal end of the wound so as to avoid leaving behind tissue with impaired blood supply as tissues farther proximalward are excised.

6. REPAIR OF INJURED STRUCTURES

How far one should go toward repair of injured structures depends first of all upon whether one can reasonably expect healing by primary union. The character of the first aid treatment that has been given, the time that has elapsed since the injury, the character and extent of the wound, the condition of the patient, the time and facilities available for repair must all be taken into consideration.

The way in which first aid treatment has been given is of great importance. The danger of inoculating the open wound with virulent organisms from the mouth and nose of unmasked first aid workers has been stressed above. So much importance do we attach to this potential source of infection that we are unwilling to consider wound repair and closure

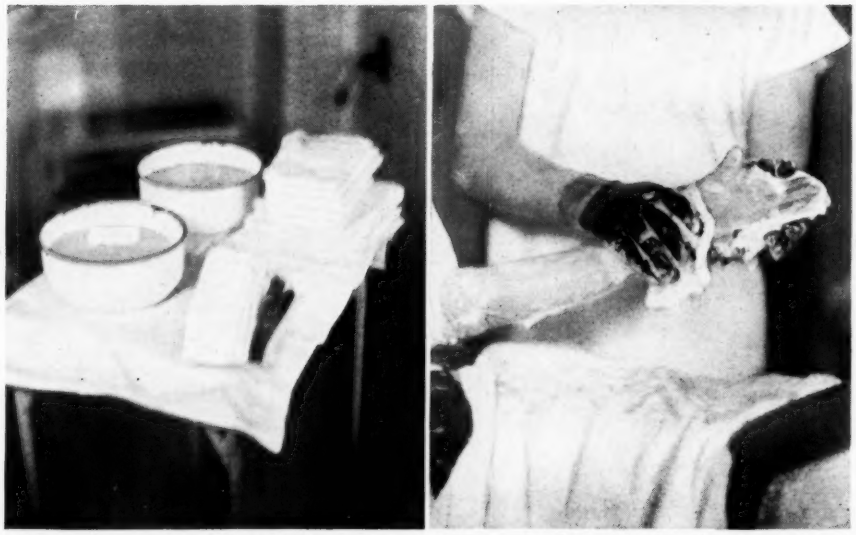


Fig. 9. Preparation of the field of operation. a, A small table, with two basins of sterile water, soft sterile cotton, a cake of plain white soap, a towel and dry sterile gloves, is ready beside the operating table. b, Cleansing of the field of operation is gentle, but thorough and painstaking, and is continued for at least 10 minutes.

Fig. 10. Lacerated wound of hand with division of extensors pollicis longus and brevis, abductor pollicis longus, thenar muscles, capsule of metacarpophalangeal joint of thumb, both digital nerves of thumb, flexor tendons of index finger and digital nerve on radial side, and flexor tendons and both digital nerves of little finger. The thumb was attached to the hand only by a pedicle of skin and subcutaneous tissues in the web. Immediate soap and water cleansing, repair of divided structures and closure of wound without drainage. Primary union. (Patient of Dr. Michael Mason. *West. J. Surg.*, 1937, 45: 247.)

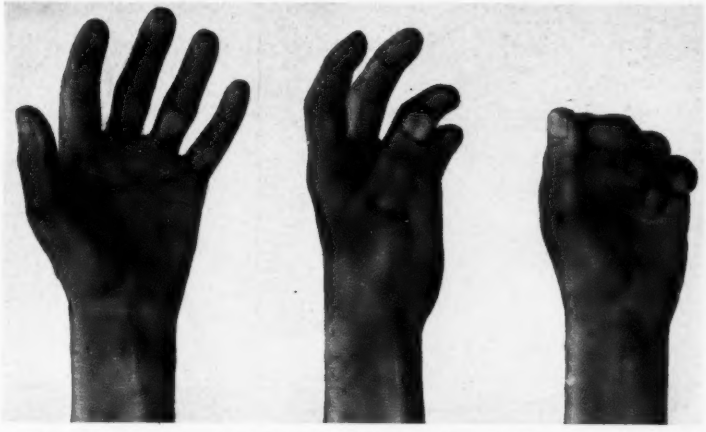


Fig. 11. Result 3 months after repair of injury shown in Figure 10. (Patient of Dr. Michael Mason. *West. J. Surg.*, 1937, 45: 248.)

Fig. 12. Crushing injury of hand with compound fracture of thumb and destruction of skin over dorsal surface of middle and distal phalanges of index finger. Immediate cleansing of wound and primary closure with sutures and skin graft. (Patient of Dr. Michael Mason. *Indust. M.*, 1941, 10: 48.)

if bleeding vessels have been tied and any effort made to "disinfect the wound" under conditions of which we cannot know. Time and again we have seen extensive wounds heal by primary union when the first aid care was limited to the application of a sterile dressing, and subsequent care given under favorable conditions (Figs. 10 to 14). On the other hand the few serious infections we have encountered as a complication of open wounds have developed in patients who were first treated in hospitals or offices which specialized in "Emergency Surgery; 24 hour service," where the use of masks was the exception rather than the rule, and where the surgeon relied chiefly upon antiseptics and upon sulfonamides in order to combat potential or already developed infection.

Fig. 13. Appearance of hand shown in Figure 12 at primary dressing 2 weeks after injury and 3 months after injury. (Patient of Dr. Michael Mason. *Indust. M.*, 1941, 10: 48.)

The time that has elapsed following the injury is an important consideration. Although some surgeons consider that it is permissible to close an open wound at any time

a b c d

Fig. 14. Crushing lacerated wound of hand with division of extensor tendons of middle and ring fingers. Immediate soap and water cleansing; suture of tendons and repair of wound 1 hour after injury; primary union. a, Before operation. b, c, d, Functional result 10 weeks after repair of injury.

Fig. 15.

Fig. 15. Crushing injury of the hand treated by immediate soap and water cleansing, wound repair and immediate covering of the extensive raw surfaces with grafts of intermediate thickness. (Patient of Dr. Michael Mason. *N. England J. M.*, 1941, 225: 108.) Above, Appearance of the hand before operation. Below, Appearance of the hand at the primary dressing 14 days after operation.

Fig. 16. Hand shown in Figure 15 as it appeared bandaged with moderate pressure and immobilized on aluminum splint during postoperative period. (Patient of Dr. Michael Mason. *N. England J. M.*, 1941, 225: 109.)

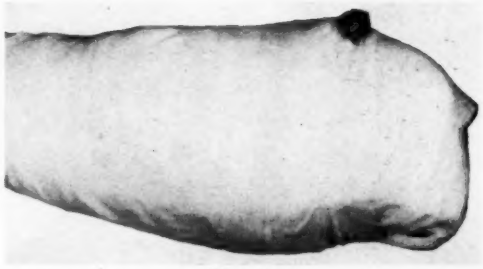


Fig. 16.

Fig. 17. Crushing injury of dorsum of hand with loss of covering tissue and exposure of extensor tendons. (*Surg. Gyn. Obst.*, 1941, 72: 166.)

within an 8 hour period after an injury has been sustained we are unwilling, except under unusual circumstances, to consider the safe period longer than 2 to 3 hours. It is possible that with the aid of the sulfonamides the "safe interval" will be increased, but there can be no question that with each passing quarter hour the chances of transforming the contaminated wound into a clean wound and securing healing by primary union are definitely diminished.

The character and extent of the wound are important considerations. Clean cut, incised wounds made by glass or sharp metal are of all least likely to be contaminated and may lend themselves to repair and closure quite as well as the purposeful incision made by the surgeon. At the other end of the scale are the extensive crushing injuries with loss of covering tissue and ragged lacerations of fascia, muscles, tendons, and nerves, and often with multiple comminuted fractures of bone. To draw hard and fast lines is impossible. Patience, gentleness, and care, combined with good surgical judgment can often accomplish some degree of restoration in limbs that seem irretrievably lost (Figs. 15, 16, 19, 20).

Little need be added concerning the importance of the patient's general condition, and of favorable conditions for carrying out difficult surgical procedures. It can be summed up in the simple statement that there is no substitute for good surgical judgment. If the patient fails to survive, the surgeon's best efforts go for naught. If the surgeon does not have adequate assistance and proper equipment the care of even simple injuries becomes exceedingly difficult and the results of treatment are correspondingly unsatisfactory.

It should always be remembered that if repair is attempted and infection supervenes little is ever gained, and the result may be disastrous. On the other hand, if one makes

Fig. 18. Result of immediate application of grafts of whole thickness skin to fill defects resulting from crushing injury of hand shown in Figure 17. (*Surg. Gyn. Obst.*, 1941, 72: 167.)

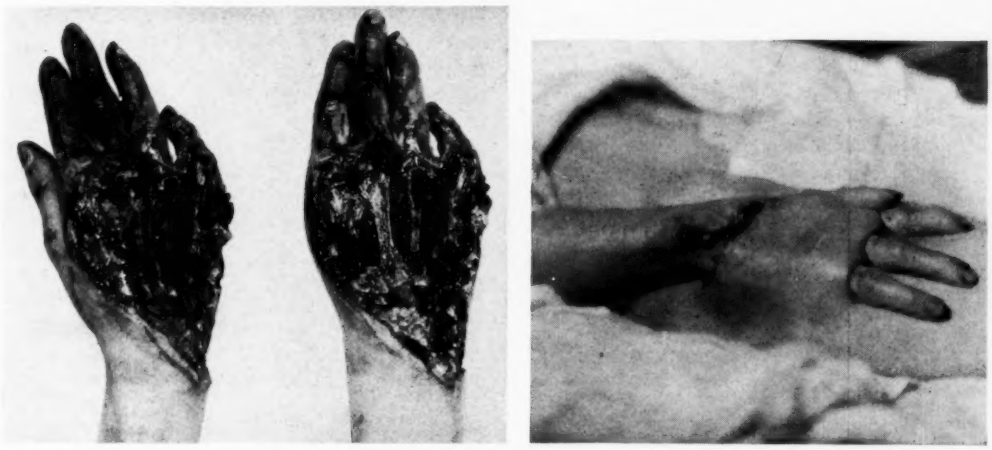


Fig. 19. Crushing injury of the hand with destruction of covering tissues, tendons, and part of metacarpal bones, treated by immediate soap and water cleansing and early application of pedunculated flap from thigh. Left, appearance of the hand immediately after injury was sustained Right, appearance of the hand underneath flap. (Patient of Dr. Michael Mason. *J. Am. M. Ass.*, 1936, 107: 1047.)

every effort to convert the contaminated wound into a clean wound and stops there, healing may follow promptly, and repair under the most favorable conditions becomes possible within 3 or 4 weeks' time.

Specific mention must be made of injuries with loss of covering tissue, injuries of blood vessels, injuries of bones and joints, injuries of nerves and tendons.

Loss of covering tissues. With avulsion injuries and loss of covering tissues the hours immediately following injury are of vital importance, for unless one seizes the opportunity to convert the contaminated wound into a clean one and close it within a few hours of the time of injury the possibility of securing the most favorable result is irretrievably lost. A razor graft of intermediate thickness (Figs. 12, 13, 15, 16), a graft of whole thickness skin (Figs. 17, 18), a sliding flap or a flap from a distance (Figs. 19, 20) may meet the indication in any particular case; the important consideration is that such a procedure, if carefully carried out, has every chance of success during the early hours following injury, but if infection develops over an extensive raw surface, an almost inevitable occurrence if the wound is treated expectantly, the chance of securing a satisfactory result is greatly diminished and the opportunity to accomplish it long deferred.

The technique of applying grafts and pedunculated flaps over raw surfaces is not diffi-

Fig. 20. Appearance of hand shown in Figure 19 eleven weeks after injury. (Patient of Dr. Michael Mason. *J. Am. M. Ass.*, 1936, 107: 1047.)

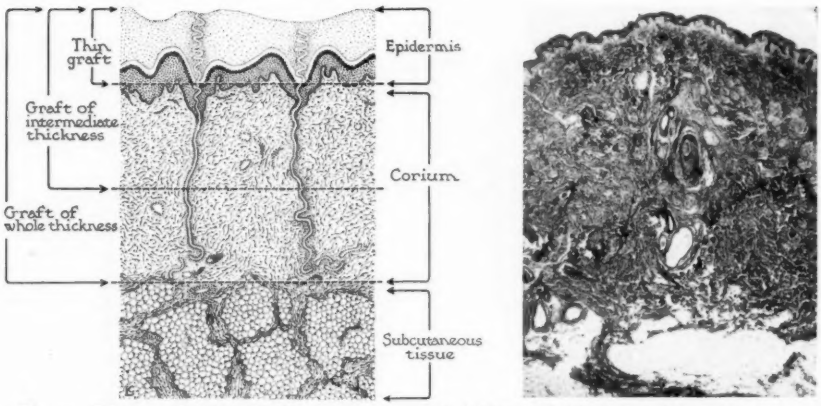


Fig. 21. Diagram showing skin in cross section, and thickness of skin included in different types of graft. In the photomicrograph of a similar section of skin, at the right, can be seen the numerous epithelial elements within the corium—hair follicle, sebaceous and sweat glands, from which the epidermis is rapidly re-formed, even though the entire epidermis and a part of the corium have been removed for use as a graft. (*Surg. Gyn. Obst.*, 1941, 72: 158.)

cult to understand or learn. Success depends on attention to a number of details which have been stressed in the many excellent contributions of Blair, Brown and Byars, J.S. Davis, and others, and well described by Webster and by Blair and Brown in Christopher's *Textbook of Surgery*.

Essential principles to keep in mind are the indications for the use of different types of grafts, the importance of covering the raw surface completely, of maintaining pressure over the graft or flap to prevent oozing underneath it and congestion within it, and the necessity for maintaining the part at rest until healing is complete.

Concerning the indications for the three types of transplants commonly used (Fig. 21), namely, grafts of intermediate thickness, grafts of whole thickness skin, and pedunculated flaps, one should remember:

1. It is wise to use the simplest procedure that will give the desired result.

2. If one can secure *prompt and primary healing* of a large open wound a covering which may not be ideal from the standpoint of appearance and function can be replaced at a later date and with the maximum chance of securing a good result. If large wounds are left open to become secondarily infected, and if deep and widespread fibrous tissue formation takes place it may be quite impossible ever to accomplish a satisfactory result, even with skillful care and multiple operations.

3. If the raw surface has a fairly normal blood supply and if structures *which require a covering of subcutaneous tissue*, such as tendons, nerves, large blood vessels, bones and joints, are not exposed in the open wound the graft of intermediate thickness is the one of choice. It can be quickly obtained with a razor or large microtome-like knife; it can be held in place with a minimum of sutures, and the raw surface left by its removal heals in 12 or 14 days if only it is covered with a nonadherent dressing, a mass of sterile gauze, bandaged snugly and left undisturbed during the period of healing.

4. If structures which require a covering of subcutaneous tissues as well as skin are widely exposed, so that they cannot be covered by drawing over them subcutaneous tissue from either side, one must provide a pedunculated flap from the adjacent tissues or from a distance. We know of no way of transplanting a graft of skin and subcutaneous tissue. Even a graft of intermediate thickness cannot live if laid over avascular structures such as tendons, nerves, arteries, and bone. That it would not be satisfactory from the standpoint of function is obvious.

5. The most frequent indication for the use of the whole thickness graft is in the repair

of freshly made raw surfaces which are surgically clean, such as result for example from excision of healed burn scars; of surfaces where a covering with minimum tendency to contract is essential (flexor surfaces); and of surfaces where a maximum thickness of skin is needed to give protection and adequate function.

With favorable conditions, namely, an open wound with base of fairly normal subcutaneous tissue, a patient seen shortly after injury was sustained, and with adequate time and facilities for carrying out an exacting surgical procedure and where whole thickness skin is needed for good function and normal appearance the use of a whole thickness graft is indicated in the treatment of a recent open wound. With less favorable conditions one would use a graft of intermediate thickness.

Closure of the open wound and healing in the minimum period of time are the objectives to keep in mind.

Injuries of the blood vessels. The control of bleeding and the treatment of shock do not come in the province of this discussion but it may not be amiss to repeat the importance of carefully applied compression over a bleeding wound, and the fact, sometimes forgotten, that pressure held directly over the site of bleeding can effectively control severe hemorrhage whereas a large mass of gauze, even if held by a very tight bandage, may fail completely to arrest the bleeding.

Of all peripheral injuries none can so quickly and certainly test the skill and equanimity of the surgeon as injuries involving the blood vessels. To grasp in artery forceps a seemingly inoffensive and fairly superficial foreign body and to have its removal followed by a gush of blood that completely deluges the operative field is an experience not easily forgotten. Only one such accident is enough to make the surgeon view every foreign body in neck or extremity with grave suspicion, to check carefully for signs of vascular injury and *in case of doubt to expose the involved area by an adequate incision above and below the foreign body before attempting its removal.* Care to secure adequate exposure is essential in every type of operation, but nowhere is it more important than in wounds of blood vessels.

Little can be said in a limited space about the difficulties that confront the surgeon in operating on a tense swollen leg, or shoulder or buttock, in which x-ray examination shows a deeply embedded foreign body and in which the tension, the bluish discoloration and the constant trickle of blood from a small wound of entry indicate the presence of vascular injury. The blood pressure cuff as a tourniquet, if a tourniquet can be applied, has the advantages of known compression, of causing minimum trauma to the tissues it surrounds, and of ease of application and reapplication. If after release of the constriction furious bleeding again takes place the cuff can be quickly reinflated and constriction re-established with minimum difficulty. An adequate incision above and below the wound is essential. Good lighting, steady retraction, and an alert and skilled nurse assistant are invaluable aids.

When areolar tissue, intermuscular spaces, even muscles themselves are tense and discolored with dark extravasated blood and when after wide incision all the soft tissues seem to bulge outward as a dark red boggy mass a steady hand and accurate anatomical knowledge are of paramount importance. Without them the surgeon is lost.

Injuries of bones and joints. In spite of a tendency to consider the treatment of fractures as belonging in a domain of its own or as the province of the orthopedic surgeon rather than the general surgeon, the presence of a fractured bone in an open wound is like the riddle: "What animal has feathers, two legs, and barks like a dog?" The animal is the same old rooster; the bark simply makes the riddle harder. In the presence of a compound fracture or joint injury the same principles of treatment apply as in other open wounds, though the successful application of those principles is admittedly more difficult.

Thoughtful surgeons are agreed upon the importance of early reduction of fractured bones and prompt closure of joint wounds. In the presence of compound fractures the principles of first aid treatment mentioned above are vitally important. The immediate application of a sterile dressing *without probing or manipulation* can prevent serious contam-

ination of soft tissues. In first aid treatment protruding bone fragments should be left untouched; to manipulate them into proper position may result in carrying surface contamination deeply into an extremity. If the patient is to be transported for any distance, however, one must run the risk of carrying infection into the wound from without as traction is applied to the limb to escape the greater risk of injury from movement of fractured fragments.

With an injury severe enough to produce a fracture the extent of soft tissue injury is unpredictable from the appearance and extent of the external wound. The presence of nerve injury can and should be known before treatment is begun. Many a surgeon has first noted to his dismay after reduction or operation upon a fractured humerus the signs of radial or ulnar nerve injury, and has been plagued with uncertainty both as to the extent and mechanism of nerve injury. Signs of injury of muscles and tendons are difficult to elicit in the presence of a fracture; often it may not be wise to attempt it.

In recognizing the presence and extent of nerve, muscle, and tendon injury and that of vascular and bone injury at the time of operation a bloodless field is an invaluable aid. It helps to simplify the work of the surgeon, it enables him to make exact and accurate observations and to carry out definitive procedures. It conserves precious blood, and makes it possible to avoid the trauma of repeated sponging. Without a field unobscured by constant bleeding accurate reduction of a comminuted fracture and accurate repair of divided tendons and nerves are difficult at best; in some cases it may be quite impossible. The first step, therefore, in treatment is the application of a constrictor, preferably a pneumatic band such as a blood pressure cuff. The position and extent of the wound may preclude its use, but the advantages of a bloodless field are so great that it should be secured if possible.

Cleansing of the wound is carried out in the manner described. Particular care is taken to cleanse bone fragments which protrude through the open wound before they are reduced. If necessary badly soiled bone ends can be snipped away with bone biting forceps, but we have seen a complete compound dislocation at the astragalocalcaneal joint heal without inflammatory reaction although the inferior surface of the astragalus had been ground into a bed of fine black dust and cinders and after prolonged cleansing the articular surface of the bone was still partially blackened by minute fragments embedded in the exposed cartilage.

When cleansing of the surface and of the exposed wound is complete sterile linen is applied and the operative procedure indicated carried out (Fig. 22). If the external wound is small, as so frequently happens in the compound fractures of civil life, it is enlarged by vertical incision above and below the site of injury. The entire depth of the wound so exposed is thoroughly irrigated with warm salt solution until clots and débris are completely removed. If indicated, gloves can be changed and fresh linen applied at this stage so as to assure the greatest possible dègree of cleanliness. Loose, torn and fragmented muscle is cleanly excised. Only completely loose bone fragments are removed; those attached to periosteum and muscle are brought into position as accurately as possible and maintained by appropriate methods. Needless to say, if it is possible to maintain reduction of fractured fragments by traction, by the Thomas splint or one of its modifications, or by a simple plaster splint both patient and surgeon are fortunate. Whether the surgeon should use some form of internal fixation in the presence of a comminuted or spiral or oblique fracture depends primarily upon his ability to transform the wound into a clean wound. Just as in cases of nerve and tendon injury, in which the use of foreign bodies is essential to secure accurate "reduction of the fracture," if internal fixation is employed to secure the fractured bone primary healing without infection is essential for a good result.

Many bitter arguments have developed over the question of using nails, plates, screws, bands and wires to maintain accurate reduction of a compound fracture, and many and varying materials have been employed from which to construct the retaining device. Much interesting experimental work has been car-

Fig. 22. Treatment of a compound fracture of leg (Courtesy of Dr. Robert McIlvenny). a, Sterile linen placed under injured leg. b, Preparation of field of operation while open wound is protected. c, Preparation of skin around wound. d, e, Exposure of site of injury with excision of narrow margin of skin about wound. f, Exposure of fractured bone. g, Reduction of fracture maintained with aid of screw. h, Irrigation of wound with salt solution. i, Wound closure. j, Application of sterile dressing and compression bandage. k, Immobilization in plaster cast.

ried out in a search for metallic substances free from irritating effect and which do not retard growth and healing of bone. In spite of arguments pro and con it is probably fair to say that the exact type of metal used or retaining device employed is of secondary importance[1], and if internal fixation is employed freedom from infection and healing by pri-

[1]The interesting experimental investigations of Bothe, Davenport, and Beaton on the effect of tantalum on healing bone indicate that in experimental animals this metal is so completely free from irritating properties that periosteum grows over it and callus and periosteum can ensheath it as though the tantalum plate were a graft of autogenous bone.

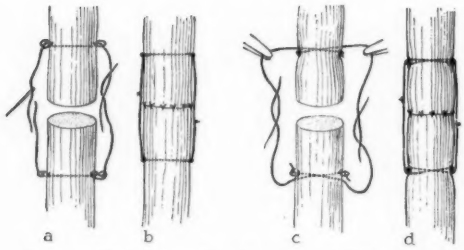


Fig. 23. Technique of tendon suture (Mason). Both methods (a, b, and c, d) are consistent with the important principle that the free ends of the two segments should be as free as possible from foreign material. Experimental studies indicate that in the second method (c, d) there is less tendency for the tension suture to cut through the tendon and permit partial separation of the sutured ends. (*Q. Bull. Northwest. Univ. M. School*, 1940, 40: 6.)

mary union are the essential factors in securing consistently successful results.

An alternative method of securing and maintaining reduction of bone fragments in a compound fracture is with the aid of pins in the ends of the fractured bone and a distraction apparatus; after reduction has been obtained pins and extremity are incorporated in a plaster cast. Orr, Anderson, and others who have advocated such a plan of treatment would take issue with the statement that this method represents an alternative method. They regard it as the treatment of choice, not only of compound fractures but of many not compounded. Without attempting to argue the question we would point out that in order to secure reduction and immobilization of a comminuted or oblique fracture with the aid of pins and distraction apparatus one must have both considerable equipment and adequate training in its use. The surgeon who is accustomed, for example, to the use of plaster or traction secured with adhesive and combined with the use of the Thomas splint may easily get into difficulties in attempting to employ a method with which he has had no experience, no matter how satisfactory the results of the method in skilled hands.[1]

[1]Recently I saw a young man with multiple injuries including a fracture at the middle of the femur. A pin for traction had been inserted just above the condyles, but too far anteriorly, so that the entire upper end of the lower fragment was drawn into a position anterior to the upper fragment. The lower extremity lay in a shining metal trough which extended only to the line of fracture and did not provide even partial immobilization of the upper fragment. The surgeon admitted he was unfamiliar with the apparatus in question, but it had been recommended as the ideal method of treatment.

Fig. 24. Simple splint for preventing constant overstretching of paralyzed lumbricals and interossei by preventing hyperextension at the metacarpophalangeal joints. A splint to prevent such overstretching should be worn for from 10 to 16 months after suture of median and ulnar nerves. (*Q. Bull. Northwest. Univ. M. School*, 1940, 40: 7.)

A second consideration is the effect of the pins upon muscles and tendons through or beside which they are passed. No one who is conscious of the restricting and constricting effect of scar tissue upon structures whose function depends upon freedom of movement can look with complete equanimity upon illustrations of pins passing through masses of muscle or through a group of tendons so important for function as the flexor tendons of the fingers.

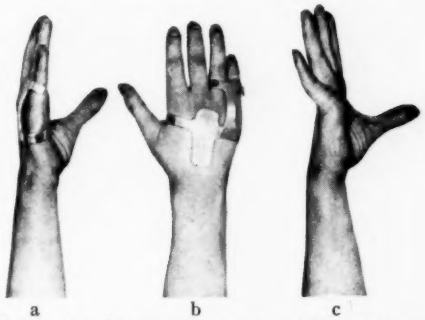
The ability of serous lined cavities to resist infection is well recognized. Joint cavities carefully cleansed and closed against access of infection from without usually heal kindly. Joint cavities left exposed to the outside

world inevitably become infected, and infection usually results in ankylosis and not infrequently in ascending infection along fascial planes and vascular channels. No one who has had experience in the treatment of extensive compound injuries would argue against the statement that care in securing complete cleanliness of the joint cavity, painstaking irrigation with salt solution, and meticulous closure of the joint capsule result in saving of joints that inevitably become infected if treated by expectant methods.

Nerve and tendon injuries. To secure good results in the repair of divided nerves and tendons it is equally essential that the wound should heal by primary union, that the operation be carried out with exacting care and that postoperative relaxation of the injured structures should be complete and maintained for from 3 to 4 weeks. It is often forgotten that not only must the patient be assured of freedom from the diffuse fibrous tissue formation that follows hemorrhage and infection, but that tendon repair must be so carefully accomplished that the possibility of gliding movement is not lost as a result of fibrous tissue formation about the site of suture; and that in the suture of divided nerves no suture material must be permitted to enter the nerve substance and lead to the scar tissue formation that blocks the downgrowth of nerve axons and makes nerve regeneration impossible.

If both nerves and tendons are injured tendons should be repaired first because they usually lie more deeply and because there should be a minimum of manipulation and disturbance of the tissues after the more fragile and delicate structures, the nerves, are repaired.

As in the treatment of bone injuries a bloodless field must be secured if possible. Tendons should be sutured end-to-end and with the finest caliber of silk which has the required tensile strength. We prefer to use untreated silk and to avoid covering it with wax or any oily material which might lessen the holding power of the knots (Shambaugh). Different methods of suture have been recommended by men particularly interested in the repair and healing of tendons. The principles that should be kept in mind are:



a b c

Fig. 25. A splint to prevent overstretching of interossei and medial lumbricals in a patient with ulnar nerve injury. a, b, Fingers supported in slight flexion at metacarpophalangeal joints. c, When the patient extends the unsupported fingers, they pass into hyperextension at the metacarpophalangeal joints and undue tension is exerted upon the muscles supplied by the ulnar nerve. (*Q. Bull. Northwest. Univ. M. School*, 1940, 40: 7.)

1. Gentle handling of tendons and avoidance of trauma are as important as in the repair of the intestine if the delicate sheath of synovial tissue which covers the tendon is to be preserved and make possible gliding movement when healing is complete.

2. To ensure prompt and sound healing there should be a minimum of foreign material (suture material) where tendon ends are brought together, so that no mechanical barrier can obstruct the growth of tendon fibers across the gap between the cut ends or divert them from a direct path from one cut surface to the other. Sutures emerging from cut surfaces, and knots lying between tendon ends constitute such barriers. A method of suture such as that suggested by Mason (Fig. 23) fulfills the requirements mentioned, for the retention suture is placed in such a manner as to leave the tendon ends free and the circular row of fine sutures, which ensures accurate apposition of cut surfaces, catches only the most superficial layer of tendon fibers.

3. The line of suture should be protected if possible with areolar tissue or subcutaneous fat to prevent fixation to neighboring structures. The more closely one can imitate the conditions normally present the more certain he will be of a successful outcome.

4. If, as a result of injury or destruction of the fibrous tendon sheaths, tendons are drawn away from the surface over which they pass

as tension is put upon them retaining ligaments must be provided to form a substitute for the injured sheaths. At times the edges of the fibrous sheath can be drawn together to hold the tendon in place, or sheath tissue still attached at one side can be drawn across the tendon and held in place by suturing its free edge. In some cases it may be necessary to provide tissue from another part of the body, such as smooth fascia or tendons that can be spared without loss of function to lay across the anterior aspect of the ankle, the dorsum of the wrist or to surround a digit. In any event the new ligament must present a smooth synovial-like surface where it crosses the tendon, it must not constrict the tendon, and it should be placed far enough from the line of suture so that the resultant callus (for tendons heal much as do bones, and with spindle shaped thickening at the line of union) does not impinge upon the retaining ligament as the tendon moves back and forth.

5. Finally, "injured tissues need rest" and the treatment of "fractured" tendons is essentially identical with that of fractured bones. *Reduction* is obtained with the aid of sutures, *immobilization* with the aid of a splint, and immobilization must be maintained *in such a position that there is a minimum of pull on the fractured fragments*. In other words, the insertion of the tendon is brought well toward the origin of its muscle and supported in such a position until healing takes place.

As Mason and Allen have demonstrated, softening of the tendon ends takes place in the days immediately following tendon suture. If movement is carried out at this stage the sutures give way from tension or cut through the softened tendon ends. At the end of 8 or 10 days, as the line of union becomes more resistant, movement results only in irritation, inflammatory thickening, and formation of adhesions. Only after the fourteenth day can gentle movement be safely begun, and then it should be only slight active movement, carried out under supervision, and still without permitting more than slight relaxation. At the end of 3 or 3½ weeks splinting can usually be discontinued and active movement carried out but with care not to put undue tension on the newly healed tendon.

Suture of divided nerves should be carried out as the final step before the wound is closed. Essential for success are accurate apposition of clean cut nerve ends with fine sutures *that do not enter the nerve substance*, freedom from tension on the line of suture, complete hemostasis, protection of the sutured nerve from fixation to surrounding structures and particularly to sutured tendons, rest of the affected limb in such a position that there is a minimum of tension on the suture line until sound healing has taken place, and *relaxation of paralyzed muscles until regenerated nerve fibers can reinnervate them* (Figs. 24, 25).

Many methods have been suggested for bridging a gap between separated nerve ends but most surgeons agree that only end-to-end suture of divided nerves can give a satisfactory result.[1] With loss of nerve substance that makes difficult apposition of nerve ends without tension the surgeon has three arrows for his bow: freeing the nerve from areolar tissue or neighboring blood vessels above and below the site of injury; bringing the limb into flexion so that the nerve passes across an arc instead of along an extended flat surface; transferring the nerve to a new position so that it traverses a shorter course. Transfer of the ulnar nerve from behind the medial condyle to the volar surface of the elbow is a familiar example of the last maneuver.

Clean cut nerve ends should be brought together without tension, and held with fine silk sutures that catch only the epineurium. Eight-o silk, swaged on a fine round needle, such as the ophthalmologists use for cataract operations, is an excellent material for suture. If three or four sutures are inserted before any are tied, their insertion is made easier and there will be less likelihood of the first sutures cutting through the fragile epineurium as the nerve ends are drawn together. The sutures so placed are then used to rotate the nerve first clockwise and then counterclockwise until sufficient sutures have been inserted to give as smooth and complete apposition as possible.

The line of suture and the adjacent portions of the nerve are protected as well as possible

[1]Favorable results with nerve grafts have been reported by Bunnell and a few others. The operation is difficult from a technical standpoint, its possibilities are not yet clearly defined, nor have the best methods of procedure been determined.

with areolar tissue from the neighborhood, with fat from the subcutaneous tissue of the open wound or subcutaneous fat from another part.

The importance of keeping the part at rest and the limb in such a position that there is a minimum of tension on sutured nerve ends until sound healing takes place is well recognized. Firm union requires from 3 to 4 weeks and no active movement that might cause tension should be permitted during this period. Equally important considerations, namely that after motor nerve injury *paralyzed muscles must be supported in a position of relaxation until regenerating nerve fibers can again make their way into them* and that their nutrition must be maintained by simple physical therapy, are too often forgotten. As a result paralyzed muscles are constantly overstretched by healthy and sometimes powerful antagonists and return of muscle tone and contractile power in the wasted and overstretched muscle fibers becomes impossible.

7. REST OF INJURED TISSUES

The oft repeated aphorism of Hugh Owen Thomas, "Injured and inflamed tissues need rest," is just as true today as it was 90 years ago. Every surgeon agrees that injured bones need rest. It is often forgotten that the same factors that favor healing of fractured bones work in an identical fashion to bring about healing of fractured soft tissues.

Every medical student knows that to secure healing of a fractured bone he must reduce the fractured fragments, immobilize the affected extremity and maintain immobilization in such a position that there is a minimum tension upon the fractured fragments. Experienced surgeons sometimes forget that the same principles of treatment must be carried out if one is to secure prompt healing of fractured tendons, nerves, and soft tissues.

A second factor in aiding healing, one that has been discovered and forgotten again and again, is that of moderate compression, uniformly applied over the wound area.[1] The helpful effect of compression is no better exemplified than in the experiences of Orr and Trueta with the use of casts completely enclosing fractured limbs and left undisturbed for long periods of time. Their emphasis upon the harm that results from cutting windows in casts is well known. Thoughtful surgeons have emphasized the fact that the essential factors in the success of Orr and Trueta's method are in continued and uninterrupted rest, the helpful effect of moderate pressure over the injured tissues and freedom from exposure of the wound to repeated bacterial contamination (Wilson).

Uniform pressure over injured tissues has at least two important advantages: it checks and limits persistent oozing of blood and serum into the soft tissues, just as sponge pressure over an oozing surface stops bleeding; secondly, it provides a substitute for the injured outer covering of fascia and covering tissue, whose integrity is so important a factor in maintaining the normal circulation in the soft tissues. Needless to say, the compression must provide moderate tension; it must be uniform; it must not cause constriction.

8. CLEANLY SURGICAL CARE

This principle, so obvious in its importance, is often forgotten—because of lack of time, because of shortage of personnel, many times because the care of wounds is entrusted to individuals not trained to accept such responsibility. One fundamental reason for the lack of trained personnel lies in our methods of training of medical students. Too often the senior medical student is overwhelmed with lectures and clinics devoted to complicated, perhaps unusual conditions, and he completes his course without knowing how to apply a dressing over an open wound without adding further infection to the wound and without contaminating himself and many of the ma-

[1] In this connection the following quotation from a recent paper by Colebrook is of great interest. "... there is one aspect of wound pathology upon which great stress was laid by Almroth Wright and Fleming during the last war, namely, that every wound produced by violent injury is really a honeycomb of 'dead spaces'—spaces between muscle bundles, in the subcutaneous tissues, fascial planes, etc.—and these spaces inevitably become filled with serous fluid which is an extremely good culture medium for certain pathogens, the commonest being staphylococci.

"Until recently we had no means of changing that congenial medium in the dead spaces into an uncongenial medium."

Colebrook's suggestion is that the sulfonamides provide the means. It is our belief that the use of pressure to prevent the extravasation and accumulation of serum in the intercellular spaces is of primary importance in aiding recovery. That pressure can also aid in hastening the return of extravasated serum and plasma into the circulation is indicated by Patey and Robertson's experiences with the use of positive pressure with a pavaex apparatus in the treatment of crushing injuries of the limbs.

terials with which he is working. He remembers bacteriology as a subject which robbed him of time and energy during his second year, but not as an integral part of surgery.

When a ward of surgical patients is entrusted to such an individual[1] it is hardly surprising that once the green discoloration of pyocyaneus infection appears on one dressing very little time elapses before the dressings of every patient with an open wound are stained with the same bluish green color. If the bacteria whose presence is so obvious are quickly carried from one patient to another it is only logical to conclude that the much less obvious but much more dangerous organisms are transmitted in the same fashion and with disastrous results. The patient who is slowly and painfully building up immunity to the organisms he has been harboring for days or weeks may be quite overwhelmed by the new and symbiotic action of fresh invaders to which he can offer little resistance.

What are the essential factors in cleanly surgical care? Tightly closed lips—still better, a masked mouth and nose; clean hands, clean instruments, "forks, not fingers."

To care for a number of patients quickly and efficiently a well equipped dressing cart is essential. A swinging tray can be quickly covered with a sterile towel; on it are laid the sterile instruments and dressings needed for the patient in question. The bandage is cut, the dressing lifted off en masse, wrapped in newspaper and placed immediately in a closed metal container attached to the cart. The wound is cleansed, if necessary, with sponges moistened with soap solution and dried with sterile gauze. Sutures are removed, dressings reapplied.

The whole procedure is carried out with sterile instruments and nothing is touched with hands or fingers until the outer bandage is applied over the sterile dressings.

Needless to say dressings are done when there is as little commotion in the ward as possible. Sweeping, bed making, visitors moving back and forth, all stir up air currents and dust and may cause further contamination of an exposed wound.

De Lee, the distinguished obstetrician, often talked to his students about an "aseptic conscience." It is one of the fundamental elements in cleanly surgical care—the care that provides for the patient in the surgical ward the same meticulous attention to details that is insisted upon in the operating room to safeguard him from the ever constant threat of infection.

[1]Said a member of a local draft board to a surgical resident recently, "Doc, we don't care how well trained you are. All we want to know is that you're an 'M.D.'"

EDITOR'S NOTE: The second and final chapter of this paper will appear in the next issue of the journal.

THE MYSTERIOUS MIXED TUMORS OF THE SALIVARY GLANDS

JOSEPH McFARLAND, M.D., Sc.D., Philadelphia, Pennsylvania

SOME years ago a group of men congregated in the lobby of this College of Physicians, and chatting upon various topics, began to talk about the various kinds of public speaking in which doctors engage. All had lectured to students, all had made after dinner speeches, one or two had lectured to women's clubs or other social organizations, some had promoted the sale of liberty bonds during the last war. Most unexpectedly one said, "Did any of you ever hear me preach?" whereupon another turned to him and said, "I never heard you speak, when you did not preach."

I shall not only lecture to you tonight, I shall preach to you, and it shall be from a text taken from the moral maxims of Josh Billings, "*You'd better not know so much than know so many things that ain't so.*"

Let us consider the subject, therefore, with reference to the things that we know, but which often, alas, "ain't so."

WHAT ARE MIXED TUMORS?

It is difficult to know exactly what we are talking about and to be sure that each knows what the other is thinking about when we speak of mixed tumors. Stedman's *Medical Dictionary* defines a mixed tumor as "one composed of two or more kinds of tissue." That is entirely inadequate for every adenoma and every carcinoma is composed of the parenchymal epithelial tissue and the interstitial connective tissue that holds it together, and in addition to these two, there is always the vascular tissue by which it is nourished, and there are a few nerves. Whatever else it may contain, every mixed tumor seems to consist primarily of the parenchymatous and interstitial tissues.

Annual conversational meeting "Lecture" before the Pathological Society of Philadelphia, April 9, 1942.

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The parenchyma may be so scanty as to be overlooked unless sought for, or it may seem to make up the entire tumor. It may consist of what can be divided into acini and ducts, but never resembles the salivary gland structure so closely as to be mistaken for it, or, as the tumor is always surrounded by a definite capsule, to suggest connection with it.

The interstitial element varies from mucilaginous substance so soft as to lead the operating surgeon to suppose that he is removing a cyst instead of a tumor, to dense cartilage-like substance containing indefinitely circumscribed masses of bone.

It is the different proportions of the parenchymatous and interstitial tissues and the condition of growth, quiescence or retrogression of each, that determine dissimilarities among the tumors.

There seems to be a world of difference between a tumor so soft and fragile as to be thought a cyst and one so uniformly cartilaginous as to be called chondroma; between one whose atypically arranged epithelial elements present a pattern like carcinoma and one whose almost purely spindle cell structure immediately suggests sarcoma. Yet they are but varieties of the same tumor.

FROM WHAT DO THE MIXED TUMORS ARISE?

In what do they begin, remembering that we are considering only those of the salivary glands—parotid, submaxillary and sublingual,—and not those of the lacrimals, hard and soft palates, face or extremities? Of 413 tumors in my collection, there were 389 parotid, 12 submaxillary and 12 sublingual.

The tumors were first described by Virchow who in 1863 spoke of them as "enchondromas" or "diffuse enchondromas," and conceived them to be of mesoblastic connective tissue origin. As they always contained some epithelial elements that had to be accounted for,

he described them as "zusammengesetzte Geschwülste" which was translated "mixed tumors."

In 1879 Wartmann conceived that the polyhedral and epithelium-like cells were really of endothelial origin. This idea was immediately adopted by Volkmann whose paper regarding the subject produced such a profound impression that the tumors were for a long time spoken of as "endotheliomas." But in 1899 Hinsberg combatted this view, and as he was vigorously supported by Borrmann, the endothelial origin hypothesis lost ground and fell into disrepute until it is seldom mentioned at present.

In 1908 a new idea was propounded by Krompecher who believed that the mixed tumors should be included among those arising from the basal cells of the stratified squamous epithelia, and who renamed them "basaliomas."

But, by whatever theory the parenchyma might be accounted for, no solution of the varying interstitial substance was reached. Virchow was greatly perplexed by the frequent presence of the cartilage, which he found to be localized in "islands" in the parotid tumors, diffused in the submaxillary tumors, and which he never found in any pancreatic tumors. He suspected that it might be a product of the capsules of the tumors, but could never prove it. Volkmann was not at all troubled by the cartilage which he conceived arose, like all of the other elements, "through the unlimited reproductive and metaplastic versatility of the endothelium."

As early as 1878 Marshall, in studying the cranial development of the embryo chick, observed that some of the ectodermal cells of the neural crests of the cephalic region contribute to the formation of mesenchyme, and Clementz seized upon the phenomenon to account for the occurrence of the epithelial elements in the mixed tumors.

Ehrich in 1906 described a mucoid degeneration of the epithelial cells of the salivary gland tumors into a soft jelly-like substance whose subsequent condensation, inspissation, and chemical transformation resulted in cartilage. Author after author accepted his view, until now it is the most popular one.

With the genesis of the cartilage (it is no longer regarded as cartilage but as a related substance called chondroid) explained, there was no longer any reason to seek for any other origin for the tumor except the salivary gland itself, and the recent French writers, Leroux and Leroux-Robert, heartily support such origin. One cannot let the matter pass, however, without reminding himself that the acknowledged exemption of the pancreas from mixed tumors becomes, thereby, more difficult to explain. It would seem as though there should be some definite reason for the appearance of mixed tumors in the facial and salivary glands and their absence from the abdominal salivary gland. Can there be a mistake in the supposed "anlage" or primordium from which they grow?

In 1877 Cohnheim expressed his opinion that the most reasonable explanation of tumor origin was the assumption that "In an early stage of embryonic development, more cells are produced than are required for building up the part concerned, so that there remains, unappropriated, a quantity of cells—they may be very few in number—which, owing to their embryonic character, are endowed with a remarkable capacity for proliferation." Let me impress upon you, without further tedious quotation, that Cohnheim believed that tumors arose from these "superfluous embryonal *cells*," and not from the frequently formed tiny supernumerary organs whose formation depends upon the dislocation of some of the substance of the developing organ. The supernumerary organ progresses in development *pari passu* with the main mass as well as it can. I often hear such referred to as "Cohnheim's embryonal vestiges," which is entirely wrong, for they are neither embryonal nor vestiges, and have no more to do with tumors than the organs of which they should have formed a part. The Cohnheimian embryonal material is cellular and usually invisible, and he believed that at any time, through some kind of stimulation, these potential but latent cells might be induced to grow, and a tumor mass, simple or complex, atypical because of its unnatural environment, might form. This fascinating theory accounts for many tumors better than any other.

Cuneo and Veau, in 1900, after a careful study of the embryology of the neck and of about 50 cervical tumors, arrived at the conclusion that "the tumors arose through local defective development of the parts in which they occurred, as the result of 'enclavement' or isolation or sequestration and the subsequent vegetation of the embryonal material." Their name for mixed tumors was "enclavoma."

Forgue and Massabuau found that the sequestered embryonal cellular material arose in close relationship to the branchial arches and therefore preferred to describe the tumors as "branchiomas."

Chevassu, more conservative in his views, conceived that mixed tumors might arise in at least 4 different ways: (1) From the tissue of a salivary gland, (2) from its embryonal glandular rudiments by "enclavement," (3) from the branchial arches (Virchow had tried to derive the cartilage in the tumors from Meckel's and Reichert's cartilage), and (4) from "embryoma juxtasalivaire" as suggested by Forgue and Massabuau.

The results of all of these theories is a nomenclature that is more mixed and more confusing than the tumors themselves. Tumors are indexed and classified by different pathologists as mixed tumors, chondromas, sarcomas, myxomas, enclavomas, branchiomas, adenomas, adenocarcinomas, carcinomas, and sarcomas, as they adhere to some one theory of origin. Or, abandoning all these classifications, the pathologist may name the tumor in correspondence with its histological structure and apparent clinical potentialities.

WHAT IS THE FREQUENCY OF THE MIXED TUMOR?

If you think, as I so often hear it said, that mixed tumors are "common," you think something else that "ain't so." In the course of some 25 years, during which time I have let it be known among my friends that I desire to study as many cases as possible, I have been able to find about 400 so called mixed tumors. I say "about 400" because the number varies from day to day as new additions come in and as cases thoroughly studied may be found to belong in some other category.

I have already explained in previous publications that my chief method of finding cases is to visit the laboratories of one hospital after another, ask permission to examine such microscopic slides of salivary gland tumors as may have accumulated, select the ones that conform to the taxonomic requirements, and then review the protocols of the cases for the essential clinical information. An arrangement is then made by which the cases are carefully followed up by the hospital office or through personal correspondence. My collection contains cases with whose microscopy I am familiar from personal observation, but it also contains a few cases very well known clinically, of which no sections are now available.

It is unusual for a protocol upon a mixed tumor to give complete details. On this account, in tabulating the tumors, the numbers appearing in one table never correspond with those in some other table. For example, if one desires to know the relative frequence of tumors on the right side or left side, out of 400 protocols perhaps only 300 make any mention of that point; if one desires to know whether the patient was white or black, no mention is made of the color in 250 cases, and so on. Sometimes the protocols, otherwise sufficiently full in detail, differ in such manner as to make case comparisons difficult. For example, when 2 repeatedly recurrent cases are to be compared, 1 protocol carefully mentions the exact time at which each recurrence was discovered, but the other protocol only records the dates of the operations for tumor removal.

My cases are all "original cases" in that no one else has ever published them; most of them remain "original cases" for anyone who wants to publish them, for with the exception of a very few cases, some of the details of which it was necessary to give, the uses I have made of them are only collective and analytic.

About 385 of my patients came to operation in various hospitals in and about Philadelphia. The remainder came from sources outside of Philadelphia; the microscopic slides and clinical data being sent to me by kind friends.

The cases have come from a total of 29 hospitals; 18 Philadelphia hospitals account for 385. Six Philadelphia hospitals account for 310: the Hahnnemann Hospital had 34; Jefferson Hospital, 72; Lankenau Hospital, 56; Pennsylvania Hospital, 34; Philadelphia General Hospital, 50; and University Hospital, 64.

If the total number of cases is divided by 6, there is an average of 51+ for each hospital. The remaining 75 cases are to be divided between the remaining 12 Philadelphia hospitals, making an average of 6+ each. Four of these 12 hospitals had only 2 cases each. Many Philadelphia hospitals had not a single case of this kind.

I was much surprised to see how rare these tumors really are, and still more so when I found that these cases were all of their kind that had occurred in these hospitals during a period of about 25 years. The number of cases was therefore reduced to 15 a year when divided among all of the hospitals of Philadelphia.

This certainly shows that the tumors are far from common, and my results are fully supported by the experiences of others. Schreiner and Mattick, in analyzing the records of 6,695 patients accepted for treatment at the State Institute for the Study of Malignant Disease at Buffalo, New York, found only 66 cases of tumors of the salivary glands. Ahlborn of the Radiumhemmit in Stockholm, Sweden, reported a series of 254 cases; Houck found 48 tumors of the parotid, submaxillary, and sublingual glands in the files of the University of Virginia Hospital, of which 6 proved to be other than mixed tumors. Leroux and Leroux-Robert (14) collected 102 cases of mixed tumors of the salivary glands and palate from material sent from various sources to the Faculty of Medicine for diagnosis. Dawson and Innes of the Research Laboratory of the Royal College of Physicians, Edinburgh, the Cancer Control Organization of Edinburgh and Southeast Scotland, and the Institute of Animal Pathology, University of Cambridge, in their collection of 316 cases, had 253 of the salivary glands. They also mention 5 mixed tumors which occurred in dogs, though in what organs the tumors occurred is not stated (8, p. 277). All this certainly shows that these tumors are not common.

Very little interest seems to have been taken in the patients from whom the tumors were removed. A number of the smaller hospitals have no follow-up service at all, and in a number of the larger ones it is inadequate; after the patient reports that he is well for a year or two he is forgotten. It seems extremely rare for the follow-up to be adapted to the particular condition for which it is intended. Mixed tumors may recur after many years so patients from whom they are removed should be followed up for the remainder of their lives. Failure to keep in touch with operation cases leads many surgeons to assume successes to which they are not entitled, and when the known facts seem to favor one as opposed to another, the former is apt to assume an attitude of superiority and explain his supposed success as the result of the thoroughness of his method, whereas, were the real facts known, there would be no difference in their results.

I have frequently been amused to hear surgeon friends speak of mixed tumors with the greatest familiarity as though they had operated upon hundreds of them. Indeed, until I came to know the facts, I supposed that to be the case; then I was both interested and astonished to find that:

At the University Hospital the 57 patients had been operated upon by 9 surgeons; average, 6.3 each. At the Jefferson Hospital 67 patients had been operated upon by 23 surgeons; average 2.0 each. At the Hahnemann Hospital 32 patients had been operated upon by 16 surgeons; average, 2.0 each. At the Lankenau Hospital 43 patients had been operated upon by 10 surgeons; average, 4.3 each. At the Oncologic Hospital 8 patients had been operated upon by 2 surgeons; average, 4.0 each. At the Pennsylvania Hospital 26 patients had been operated upon by 13 surgeons; average, 2.0 each. Or, if we consider the total, 233 patients from all hospitals were operated upon by 73 surgeons, an average of 3.2 cases each. But 37 of the 73 surgeons mentioned had only 1 case each, and 13 more had only 2 cases each.

In all of the hospitals from which our material was gathered, there were only 6 surgeons who were credited with 10 or more cases each, the greatest number being in the experience of the late Dr. John B. Deaver, who, at the Lankenau and University hospitals, operated upon a total of 29 patients with mixed tumors.

It is to be remembered that these figures do not represent the work of one year, but of the total period included in the research—approximately 25 years! Beware of him whose knowledge is based upon acquaintance with *a case*—he knows many things that "ain't so"!

WHAT IS THE HISTOLOGICAL STRUCTURE OF MIXED TUMORS?

That the histological structure is extremely variable is shown by the fact that Harvey, Dawson and Innes made use of 54 photomicrographs to present and explain the variety of appearance they observed. They, however, included some lachrimal, palatal, labial, molar, and mammary mixed tumors, not in the scope of the present discussion.

In the paper "Etude analytique des éléments constitutifs des tumeurs dites mixtes des glandes salivaires," Leroux, Leroux-Robert, and Dillange (15) presented 10 beautiful photomicrographs illustrating the different appearances observed in the 40 cases they studied and the following explanation: "The apparent complexity of their structure depends upon local morphological variations among cells of the same type, and not from multiplicity of cell types." In a later paper, "Essai de classification architecturale des tumeurs des glandes salivaires," Leroux and Leroux-Robert (14) used 24 photomicrographs to illustrate the varying appearances observed in 102 cases that were studied from the standpoint of histopathological prognosis. In a paper dealing with the same subject, "The Histopathologic Prognosis of Salivary Gland Mixed Tumors," I (16) used 12 photomicrographs for the same purpose. All this goes to show that the tumors have a most varied and complex histopathological structure, however it may be accounted for. Indeed with such complexity it may become difficult to decide whether a given tumor is a mixed tumor or not. In my own collection it was found necessary to eliminate 2 capillary angiomas, 2 Hürthle cell tumors (onchocytomas), 2 neurofibromas (schwannomas), and 2 branchiogenic carcinomas.

The inclusion or exclusion of such tumors must depend, in part, upon the theory of origin to which one inclines. If he follows Cuneo and Veau and Chevassu in believing that the tumors arise through the "enclavement" of embryonal substance in the developing face and neck, they may be retained; if, on the other hand, he accepts the origin of the tumors from neoplasia of the respective salivary glands, they must be eliminated. To make our studies agree with this latter, now popular view, we have eliminated them.

Leroux and Leroux-Robert (14) divided their 102 cases into 17 separate varieties, which would allow an average of only 6 tumors in a class. Of course of the more frequent varieties there were more, and in the rare varieties less, so that sometimes conclusions as to the benignancy or malignancy of a class had to be deduced from what was known about 1 or 2 tumors of a group whose clinical behavior is acknowledged to be highly variable. It is evident that the most erroneous conclusions might be arrived at! They were, however, quite justified in the creation of their categories, and for my own purposes I have found it useful to arrange the tumors in 14 groups.

It would be appropriate to show this histopathological arrangement at this point, but it seems preferable to reserve it for a later heading when its presentation may accomplish several purposes.

ARE THE MIXED TUMORS BENIGN OR MALIGNANT?

Josh Billings, if he had ever considered this subject and heard it argued about, would again remind us that those who find the question of benignancy and malignancy easy to define or agree upon, know some things that "ain't so."

Ewing, in considering the question, says, "The distinction between benign and malignant tumors involves questions of great

interest both from the theoretical and practical sides. If malignancy were a purely clinical conception it would be impossible to draw any rigid distinction between benign and malignant tumors, since nearly all tumors may occasionally prove fatal. Yet the tendency is to restrict the term to tumors which exhibit certain features which are essentially deleterious to the host. The most important of these features are (1) infiltrative growth, (2) local destructive properties, (3) recurrence after removal, (4) formation of metastasis, (5) local interference with function, and (6) general toxic action of absorbed tumor products." Taking these up in the order in which they are given, we find:

1. *Infiltrative growth.* Mixed tumors are usually definitely encapsulated, and therefore rarely infiltrative. But if the capsule is opened through traumatic accident or through surgical intervention, as is much more frequently the case, the infiltrative growth may take place as in Case 59. This tumor after 2 operations, 1 for the removal of the primary growth and the other for a recurrence, invaded the orbit causing exophthalmos, eventually penetrated the cranial cavity, and caused death by compressing the brain. Such cases are fortunately rare.

2. *Local tissue destruction.* The tumors usually project externally so that the skin is the organ most affected. Its great capacity for stretching, however, usually prevents serious accidents, and tumors of 5, 6, and 7 pounds have been observed without ulceration. The close anatomical relation of the parotid tumors to the 5th and 7th nerves results in pain or palsy in some cases, and it may be for the relief of these evils that the patient seeks advice. If the skin be penetrated because of rapid growth of the tumor or traumatic accident to it, permanent ulceration with fungation, occasional hemorrhage, and infection may follow and even be fatal. In the great majority of tumors no such accidents occur, and the famous tumor observed by Cotterhill attained an estimated weight of 22 pounds without such mishaps.

3. *Recurrence after operative removal.* Of the 400 mixed tumors that I have been privileged to study and that form the foundation of my opinions, about 100 are known to have recurred; that is 25 per cent. This is the percentage given in text-books for recurrence, though F. C. Wood found it to be 45 per cent, Benedict and Meigs, 42.5 per cent, and Stein and Geschichter, only 20 per cent. This variability may have something to do with the method of classifying the tumors, but perhaps more to do with the method of computing the percentages.

It seems very simple to say 400 cases with 100 recurrences means 25 per cent, but it is very inexact. Of the 400 cases, we have no recent follow-up record on 96 so it is not known whether they are living or dead, with or without recurrences. Eliminating them, the recurrences rise to 32 per cent. In most estimations of success or failure of operative treatment, the surgeon is content if his patient is free of disease after the "5 year period." Suppose that every one of our cases not under observation for 5 years was ruled out; then the recurrences would rise to 40 per cent. But 66 patients from whom mixed tumors have been removed have died without having shown the recurrences from which they might have suffered had they lived longer. If they are deducted so that our calculations are based only upon those patients still living and still under observation, the number of recurrences rises to 50 per cent. But even this figure, based on the 5 year period of exemption, is in error because the 5 year period does not apply in the case of mixed tumors as the average time that elapses between the removal of the primary tumor and its postoperative recurrence is 7.2 years. If we calculate on that basis, the recurrences rise to 61.72 per cent.

But again, though 7.2 years is the average interval between operation and recurrence, it will be seen that one-half of the recurrences take place after a longer period, and are sometimes deferred for 20, 30, and in 1 case 45 years. This leaves every case open to the possibility of recurrence and causes one to wonder whether any one who has been the victim of this type of tumor may ever be pronounced "cured."

Tumor recurrences may have several causes; it may be desirable to mention no more than

2. The first is a repetition of the same conditions and process by which the primary tumor was brought about, viz., an appropriate primordium acted upon by the appropriate stimulant. From that point of view the primary and recurrent tumors would be independent entities which simply appear in the same region. It would be unnecessary to mention this idea except that it is occasionally offered as an explanation of the long interval that elapses between the operative removal of a mixed tumor and its recurrence.

The more popular and probably more valid explanation is that the recurrence is only the continued growth of tumor tissue left behind at the primary operation. But while that is easy to understand in cases of cancer, in the presence of which it is well recognized that the cells penetrate into the crevices of the tissue and extend, by permeation, widely beyond the confines of the visible and palpable tumor and that the same cells enter into the lymphatics and are carried hither and yon—it is difficult to understand in the case of a circumscribed and encapsulated tumor completely removed, capsule unopened.

Another explanation, however, may suffice to clear up the subject. The tumors appear to be unicentric and probably frequently are; but many are undoubtedly multicentric, and I have sometimes seen a congeries of little tumors the size of peas or even of pinheads, in close juxtaposition to the larger easily recognized tumor. The mixed tumors are also nearly all lobulated, the various lobules are often quite different in structure or development. It is quite conceivable that these lobules began as different centers, some outgrowing others, or having started before others, and in growing larger and larger, came into closer and closer approximation, crowding out the intermediate tissue elements by pressure atrophy until, capsule coming into contact with capsule, the entire aggregation became surrounded by an additional common capsule of the tumor. If the operative removal of the tumor was attempted while any one of the smaller lobules remained separate from the whole, there would be a good chance of its being left behind to appear later as a new and recurrent tumor. Should this suspicion be true, it ought to be capable of producing some proof, and so I (17) carried out a study on the recurrences of the tumors with special reference to their size at the time of operation. Theoretically, the smaller the tumor at the time of removal, the more likely recurrence would be. Unfortunately the sizes were always expressed in comparison with familiar objects—peas, beans, olives, plums, eggs, apples, oranges, grapefruit, cantaloupes—not in actual measurements. But, regardless of the errors that prevent scientific accuracy, I was able to secure the figures in Table I.

TABLE I

	Cases	Recurrence	Per cent
Group I—tumors smaller than a walnut	28	9	32.1
Group II—tumors larger than walnut but smaller than lemon	109	19	17.4
Group III—tumors larger than a lemon	19	2	10.0
As group III is so small and contains only 2 recurrences, combinations were tried for comparison—			
Groups I and II—all less than size of lemon	137	28	20.00
Compare with group III	19	2	10.00
Or			
Groups II and III—all larger than walnut	128	21	16.00
Compare with group I	28	9	32.1

So it seems that however the combination is arranged and compared the smaller tumors suffer the greater number of recurrences. Since these computations were made, another 100 tumors have been added to my collection, and I have hastily reviewed them without any change in the principle or considerable variation in the figures.

The matter must not be closed, however, without calling attention to the danger of leaving part of a tumor behind at the time of operation, either through the accident of tearing the capsule of a very soft tumor or intentionally tearing it because the tumor is in such intimate relation to the facial or other nerves. Such residual tumor tissue usually results in "immediate recurrence" which, of course, is only the continued growth of the primary tumor.

The second factor that may play an important rôle in recurrence is the variety of tumor to be dealt with. One hesitates, how-

TABLE II.—CLASSIFICATION

	Cases	Recurred	Per cent	Fatal
a. Interstitial tissue tumors				
Simple interstitial tumors	97	35	36.2	0
Interstitial tumors complicated by				
Excessively cellular matrix	9	3	33.3	0
Presence of squamous epithelial cells	14	5	35.7	0
Cylindromatous hyaline change	9	6	66.6	0
Unusual number of gland-like elements	9	4	44.4	0
Scattered cell groups suggesting carcinoma	6	3	50.0	0
Appearance suggesting sarcoma	3	1	33.3	0
Presence of osteoid or osseous tissue	3	0	0	0
Total			41.2	
b. Parenchymatous tumors—canalicular or racemose tumors.				
Simple canalicular	17	9	52.9	0
Papillary intracanalicular	11	9	81.8	4
Carcinomatoid canalicular	6	3	50.0	1
Total			61+	
c. Carcinomatoid tumors	13	10	76.9	6
d. Sarcomatoid	8	2	25.0	1
Totals			51.1	12
Grand Totals	205	90	48.8	

ever, when the term "variety" is used because, should there be different varieties, it should be possible to define them and thus construct a classification. However, it will be well to forego any attempt at classification or at scientific denomination, and do no more than arrange the tumors with reference to appearances that may have no nosological value because appearances may be the result of temporary conditions of tumor growth rather than permanent qualities.

As has been pointed out, every mixed tumor consists of interstitial and parenchymatous tissues, the proportions and conditions of which vary. With these facts in mind, we can arrange our tumors in little groups (Table II) that can be readily compared with one another, if we know how many tumors in each group recurred or eventually proved fatal.

Table II shows that the interstitial tumors occur about 3 times as frequently as the parenchymatous tumors, but recur far less frequently, 41.2 per cent of the former as compared to 61+ per cent of the latter. With such an analysis before us, it might easily be assumed that the microscopic examination of a section of mixed tumor would enable one to make a reasonably correct prognosis, but curiously enough when it was tried in actual practice it did not seem to work out that way. But who knows how correct or incorrect general deductions made from the study of microscopic sections are? I decided to find out for myself, and choosing a slide from my collection at random, I noted the supposedly dependable indications of malignancy and wrote down whether I believed the tumor would recur or not. After having done this many times, I compared my opinions with the known facts and was shocked and humiliated to find how frequently my prognosis had been incorrect. A glance at Table II will show the reader that there are recurrent and nonrecurrent tumors in every group except the group of interstitial tumors complicated by the presence of osteoid or osseous tissue. Was my inability to differentiate between the tumors that had recurred and those that had not yet recurred due to my own stupidity or did it lay in the nature of the material?

To answer that question I selected sections of 50 tumors whose behavior was known up to the present time and offered them to 25 competent pathologists, 8 of whom hold professorial positions in the departments of pathology in medical schools and 8 of whom are the heads of the laboratories of large hospitals, while the others represent varying degrees of skill and experience from beginners to those regarded as ready for first class po-

sitions. They were asked to answer only one question about each tumor: "Do you think it will recur?" It was interesting to observe the attitude of the men toward the problem. Some proceeded swiftly and with confidence that they would make no mistakes, others were puzzled and reviewed their work again and again; one gave up about one-third of the slides saying that he was "unable to come to any conclusion about them."

The results were most interesting and astonishing! The average end-result was 52 per cent correct and 48 per cent erroneous. The extremes were not widely separated: the lowest percentages of correct opinions were 43 per cent, 45 per cent, and 45 per cent, attained by 2 men of professorial rank and 1 who is the head of a tumor clinic. The highest percentages of correct results were 63 per cent and 63 per cent attained by a professor of pathology and a hospital laboratory director.

One naturally inquires whether all made the same mistakes and is surprised to learn that they rarely agreed or disagreed with any uniformity. This is best shown by the results of 2 mentioned as having attained the highest marks. They fully agreed about a number of cases, concerning one-half of which they were wrong. All this is most disheartening! It does not seem possible to foretell what a mixed tumor of the salivary glands will do by examining a section of it with the microscope. Not only is that true, but accurate prognosis seems to be impossible in any case.

This brings us again to the subject of malignant tumor and curability, this time with special reference to metastasis.

4. Metastasis. Dogmatic statements concerning mixed tumors should be avoided, but it may be stated with very little reservation that metastasis is so rare that its occurrence may almost be denied. Of the 100 cases under consideration at present metastasis may have occurred in only 2. It is not certain that what were believed to have been metastases in these cases may not have had some other explanation, but they looked like metastases and are so regarded. They differ from metastasis in general, however, for in practically all other tumors, metastasis not only stamps the tumor as malignant, but also marks the approach of the fatal termination. On that account surgeons now usually refuse to operate upon patients in whom metastasis has been discovered. But metastasis in mixed tumors seems to have little to do with either malignancy or approaching death for of the 2 cases mentioned, in which it was found in the lymph nodes, 1 patient has remained well for more than 20 years, and the other for more than 5 years. More will be said upon this subject later.

5. Local interference with function. This is rarely an important occurrence in the clinical behavior of mixed tumors until they have been operated upon. What happens may depend upon the exact location of the tumor. In one position it may prevent the easy movement of the jaw and more and more restrict the opening of the mouth as the tumor becomes larger. In other cases the external auditory meatus may become compressed and unilateral deafness brought about. When the facial nerve or some of its fasciculi are caught in the growing tumor and compressed, facial palsy in varying degrees of severity may result. When branches of the 5th nerve are similarly affected, pain or actual *tic douloureux* may result. In rare cases pressure upon the duct of some part of the gland results in cystic distention.

But when the tumor is operatively attacked, cut into, or only partially removed, local invasive growth may follow with varied results, depending upon the extent and magnitude of the invasion.

6. The general toxic action of absorbed tumor products. It is doubtful whether "tumor products" ever play any part in the pathology of mixed tumors, unless the tumors that ulcerate, bleed and become infected are referred to. Patients with such tumors do not suffer from "tumor products," but from more commonplace conditions—sapremia, septicemia, and similar conditions.

From this analysis and synopsis we are left in some perplexity as to whether mixed tumors are malignant or not. A good deal of this is the result of the terminology used by different pathologists in reporting the tumors and in talking about them. One pathologist calls

them adenomas, another says "they usually turn our to be adenocarcinomas," a third will find myxomas, chondromas, and sarcomas. How much better it would be to say that they are "mixed tumors" and will probably recur.

Many also assert, as I myself once thought, that they might begin as benign tumors and afterward "become malignant." Were that true, it might be necessary to reverse the thought so as to account for the cases that begin as malignant tumors and later "become benign" as seems to be the case with some of the "carcinomatoid" tumors.

I have been challenged for my use of the word "carcinomatoid" so I hasten to explain that I use it as a caption under which to place those tumors whose histopathology is in part so suggestive of carcinoma, or so completely that of carcinoma, as to make differentiation impossible. I avoided the already familiar word "carcinoid" because it is the name of a well known tumor of the gastrointestional apparatus, arising, presumably, from a type of cell not found in the salivary glands. I do not use it with any pretention to scientific accuracy but as a convenient means of grouping certain remarkable tumors until they are better understood and explained.

The difference between the carcinomas and the carcinomatoids is impressive. In my first paper (18) I gave the criteria by which I believed it possible to recognize the *carcinomas* in these words: "When the growth is so rapid as to bring the patient to operation within a year, and the excised tissue resembles carcinoma, the prognosis is bad." I am now ready to reiterate the statement, laying down additions as follows: (1) When the preoperative duration of the tumor is expressed in months, (2) when the tumor grows rapidly, (3) when there is metastasis to the lymph nodes, (4) when the histology of the tumor is that of carcinoma, the tumor usually is carcinoma, and (5) the patient dies within a few years, no matter how carefully treated surgically and roentgenologically. That summary applies to more than a dozen cases not included in this paper because they were not mixed tumors. See how different are the facts with reference to the carcinomatoid group of tumors.

The carcinomatoids may so closely resemble carcinomas as to be quite regularly mistaken for them. They may also resemble carcinomas clinically so as to be separated with difficulty from them. I am not always certain myself whether a tumor under consideration is one or the other. But if one has all of the necessary data he will find that between carcinoma and carcinomatoid there are marked differences such as the following:

1. The carcinomatoids usually have an extremely long preoperative duration.

2. They usually appear at an early age. Case 115 first suffered from the tumor at 10 years of age. Case 127 first suffered from the tumor at 4 years of age, and Case 197 has had the tumor since childhood.

3. The course of the tumor growth is very slow. Case 115 had been treated by surgical excision, x-ray, and radium treatments for 15 years, and Case 127 had been treated by surgical excisions et cetera, for 25 years.

4. They are almost never metastatic. Case 76 had metastasis in a lymph node that was mistaken for squamous cell carcinoma and Case 115 had "mixed tumor metastasis" in a cervical lymph node.

5. They frequently "recover" (?) under treatment. Case 76, after a second excision for a recurrence about 2 years after the first, has seen no sign of recurrence in 20 years; Case 191, after a second operation, has had no recurrence in 18 years; and Case 115, after 5 excisions and 2 courses of x-ray treatments, has been free of tumor for 5 years. (She had 3 recurrences and operations for excision *after* the x-ray treatments had been completed).

THE TREATMENT OF MIXED TUMORS

As has already been pointed out, the general rule that the best way to treat any tumor is to excise it completely, as soon as it is discovered, does not apply in the case of mixed tumors. Ordinarily it has everything in its favor, for it is easier to remove a very small tumor than a very large one, and the resulting scar or disfigurement is much less. But when there is plenty of time to wait and the result of waiting is beneficial, it certainly seems wiser not to operate as long as the patient is willing to wait. In most cases the longer he

waits the better, and there is nothing arbitrary about the lemon size that I adopted in compiling the statistics of operation; orange size or grapefruit size might be better except that vascular complications are likely to present themselves when the tumors are very large. Tumors of 6 or 7 pounds have, however, been successfully removed.

It seems useless to attempt to control or modify the growth of the tumor or to postpone its recurrence by the use of x-ray or radium. I have made a special study of the subject and have published a special paper, showing that in not a single case could it be proved that any real benefit has ever been achieved.

Supposed indications for treatment are as follows:

1. The embarrassment of the patient caused by the presence of the disfigurement. This should be overcome by the argument that having already had the tumor for a number of years, it ought not be difficult to endure it a few years longer as its removal may be followed by worse evils such as salivary fistula, which is very rare, facial palsy, which is not rare, or recurrence. That is the sequel to be most dreaded and it will make other operations more difficult.

2. Limitations of the mandibular movement that make opening the mouth difficult. This is a real indication the importance of which cannot be overlooked. It may be well to remove the entire parotid gland in such cases lest there be a recurrence.

3. Pain from pressure upon the sensory nerves. This also may be a perfectly valid reason for operation, and if such treatment is instituted, thorough dissection of the entire gland is to be recommended.

4. Sudden rapid increase in the size of the tumor. Although not always possible to explain, this is usually of no importance. If the tumor is a mixed tumor, rapid growth usually supervenes after the tumor has existed for years. If the tumor is a carcinoma, its excision usually fails to afford much benefit. Every patient with carcinoma of the salivary gland who has come under my observation has died regardless of any kind of treatment, early or late, by excision, radium, or x-ray.

The results of treatment in the case of mixed tumors are impossible to evaluate. In all probability at least one-half of the recurrent cases in my collection were, and a great many still are, believed by their surgeons to have been cured. Doctors fail to follow up their cases, forgetting that 10, 20, 30, or 40 years may pass before a recurrence presents itself.

One case is cited below, to show how necessary persistent follow-up is:

Case 6, S. H., a white female, aged 23, came to the German (Lankenau) Hospital on February 5, 1910, with a tumor that was known to have been present, at the angle of the left jaw, for 7 years. Its growth had been gradual. The tumor was excised by Dr. John B. Deaver, and upon microscopic examination by various pathologists had been called "myxochondroendothelioma of the neck," "adenocarcinoma of the parotid gland," and "cylindroma."

In 1926 in my first paper, "Ninety Tumors of the Parotid Region" (18), I mentioned this case and said "The patient is now living and well after 15 years." Ten years later, in 1936, in my paper "Three Hundred Tumors of the Salivary Glands" (17), I again referred to Case 6 as having remained "without recurrence for 25 years." If any patient can be accepted as cured this should have been true of Case 6, but if you asked me about her present condition, I should be obliged to say that on February 2, 1939, I received a letter in which she said "There seems to be a growth started, just where the other one was. It is about as big as an ox-heart cherry and hurts when I press upon it." This happened 29 years after the operation!

CONCLUSIONS

The mixed tumors of the salivary glands are a group by themselves. It is impossible to be dogmatic about them for they disregard every canon of oncology and continually do the most unexpected things. It is impossible through the microscopic study of their structure, to foretell what any of them will do any variety may recur. The long delay before recurrence deludes the surgeon and roentgenologist into believing that he has been successful in his treatment, when no good at all has resulted. The same long delay and the occasional recurrence of the tumor 20, 30, or 40 years after operation justifies the question, "Is any patient, once the victim of such a tumor, ever cured?"

It seems appropriate to end where we began and say that the more we learn about the

mixed tumors of the salivary glands, the less we seem to know and *"You'd better not know so much than know so many things that ain't so!"*

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AMPUTATIONS FOR ADVANCED ARTERIAL DISEASE

A Critical Analysis of the Mortality

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THE high mortality from major amputations for arterial disease is frequently attributed to operative delay due to efforts to save the limb by conservative treatment. However, early operation does not seem warranted without first attempting to determine the course of the various factors contributing to the disease by subjecting them to treatment. Not infrequently, patients in whom early amputation seemed advisable have improved under conservative treatment to unexpected recovery. Delay in amputating, however, is not justified when the life of the patient is endangered by complications or when the limb is hopelessly involved by the disease.

This study is an attempt to evaluate the factors contributing to major amputation for advanced vascular disease and to determine whether or not delay in amputating affects the operative mortality.

MATERIAL STUDIED

During the 7 year period (1935–1941) that has elapsed since the vascular therapy department of the Presbyterian Hospital was organized, 160 patients having complete occlusion of the main artery of 226 lower extremities have been examined and treated. Forty-three of these patients had 50 major amputations (Table I). Those patients who were examined and treated exclusively in the central free dispensary of the Presbyterian Hospital are not included in this study. Within the 7 year period an additional 29 major amputations for vascular disease were performed on patients who were not seen in the department (series II). The *mortality rates* in the 2 series are given in Table I.

All the extremities in series I were found by oscillometric readings to have complete organic arterial occlusion either at the ankle, knee, or thigh. Dissection of the amputated specimens revealed that oscillometric index up to 0.3 unit may occur in the presence of complete occlusion of the main artery. Accordingly, readings from zero to 0.3 unit were accepted as evidence of complete occlusion of the main artery. (In our experience we have found the results of the oscillometric examination far more accurate than digital palpation of arterial pulsation).

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FACTORS CONTRIBUTING TO MAJOR AMPUTATION

In reviewing the records of the 50 amputation cases in series I, it is apparent that major operations were definitely indicated. When major amputation is selected the following factors were considered important:

Pain, infection, gangrene. The large majority of the amputations were performed for pain, infection, and gangrene in extremities with advanced organic arterial occlusion (Table II). Both pain and gangrene were present in over 80 per cent of the cases and infection in 60 per cent. The lesser incidence of infection may be accounted for by the uncertainty of infection in many cases. Elevation in mouth temperature may not occur or may be very slight because the deficient circulation limits toxic absorption, or, again, moderate elevation in temperature may be due to toxic absorption from gangrenous areas without the presence of infection. Bacteriological studies were not made in all cases. In the series here reported, major amputations were unquestionably necessary as evidenced by the frequency of all 3 complications—pain, infection, and gangrene.

Site of arterial obstruction. The level of arterial obstruction in the extremity affects the incidence of amputation. In the senile arteriosclerotic group (Table III), only 18 per cent of the extremities with arterial ob-

TABLE I.—INCIDENCE AND HOSPITAL MORTALITY FROM MAJOR AMPUTATIONS FOR ADVANCED ARTERIAL DISEASE

	No. of patients	No. of involved extremities	Amputations		Mortality	
			No.	Per cent	No.	Per cent
Series I.—From the Vascular Therapy Department, 1935–1941.						
Arteriosclerosis Senile	66	90	19	20.1	4	21.0
Diabetic	37	57	22	38.6	2‡	9.1
Thromboangiitis obliterans	37	53*	3†	5.6	0	0.0
Embolism and thrombosis	18	24	4	16.6	0	0.0
Popliteal tumor (no aneurysm)	2	2	2	100	0	0.0
Total	160	226	50	22.1	6	12.0
Series II. Not examined in Vascular Therapy Department, 1935–1941.						
Total			29		6	20.7

*Five additional extremities were amputated elsewhere prior to patients' coming under our care with acute involvement of remaining lower extremity.
†One amputation was performed elsewhere after the third recurrence when we refused further treatment due to patient's uncooperative attitude.
‡Both deaths followed the second major amputation (see case reports).

TABLE II.—INDICATIONS FOR MAJOR AMPUTATIONS FOR ADVANCED ARTERIAL DISEASE

	Indications for amputation			Average age		
	Pain Per cent	Infection Per cent	Gangrene Per cent	All cases	Amputation cases	Amputation hospital deaths
Arteriosclerosis Senile	73.3	66.7	73.3	68	71	78
Diabetic	89.5	63.1	89.5	58	65	59
Thromboangiitis obliterans	100	100	100	46	36	
Embolism and thrombosis	100	100	100	55	47	
Popliteal tumor (no aneurysm)	100	0.0	50	38	38	

TABLE III.—INCIDENCE OF AMPUTATION ACCORDING TO LEVEL OF COMPLETE OBSTRUCTION IN THE MAIN ARTERY

	Ankle		Below Knee		Thigh		Total	
	No. cases	Per cent of amputations	No. cases	Per cent of amputations	No. cases	Per cent of amputations	No. cases	Per cent of amputations
Arteriosclerosis Senile	43	18.6	10	60.0	9	55.5	62	30.6
Diabetic	21	47.6	16	68.7	1	100	39	56.4
Thromboangiitis obliterans	26	0.0	6	16.6	5	40.0	37	8.1
Embolism and thrombosis	3	33.5	7	28.6	7	14.3	17	23.5
Popliteal tumor (no aneurysm)	0	0.0	0	0.0	2	100	2	100
Total	93	20.4	39	51.3	24	45.8		

struction at the ankle were amputated while more than 50 per cent required amputation when the occlusion was at a higher level. It is apparent, therefore, that conservative treatment is more successful when the arterial obstruction is confined to the ankle or foot.

In the diabetic patient the incidence of amputation was very high (50 per cent) irrespective of the level of occlusion in the main artery. When amputation is being considered, the presence of extensive arterial occlusion makes it very unlikely that conservative treat-

ment will improve the condition and therefore major operation should not be unduly delayed. This report, however, does not include the majority of diabetic patients who have only peripheral arteriolar involvement. In the absence of main artery occlusion these patients have been treated successfully by conservative measures and minor surgical procedures.

The frequency of major amputations for high arterial occlusion for embolism was less than that observed when the occlusion was at a lower level. This is due to the presence of greater collateral circulation at the higher level. However, when the main artery is extensively occluded by secondary propagating thromboses there is little hope of saving the limb by conservative treatment. This fact should be given serious consideration when there is a tendency to delay operation.

Age as a factor. Advanced age in a patient does not justify continuance of conservative treatment when amputation is otherwise indicated. In those cases studied, the average age of 66 patients having senile arteriosclerotic vascular disease was 68 years; of these patients, 19 underwent major amputation. The average age in this group was 71 years and, of the 4 deaths that ensued only 1 patient was under 79 years (Table II), which fact further indicates that the patient's physiological age is a more important factor than his actual age in considering amputation.

In the other groups studied, age as a factor in deciding upon operation was of less importance. In all cases, however, patients of advanced age suffering with extensive arterial occlusion are much less likely to benefit by conservative treatment. The incidence of amputation among the arteriosclerotic patients was particularly high, as was the mortality (Table I). However, the risk in not operating upon these patients is even greater than that taken in operating.

Bilateral involvement of extremities. There is a greater tendency to delay amputation when both extremities are involved or when one extremity has already been amputated. Consequently, amputation of the second limb would be expected to involve a higher mortality. Five bilateral amputations for arteriosclerotic gangrene (7 of 44 cases of bilateral involvement required amputations) were successfully performed. Two deaths followed the second major amputation for diabetic arteriosclerosis and were due to coronary thrombosis and pulmonary embolism, respectively. These results do not support the contention that operative delay contributes to the mortality from amputations (2).

HOSPITAL MORTALITY FOLLOWING AMPUTATIONS

The 6 deaths from major amputations occurred among those patients having extensive arteriosclerosis (Table I). These operations involve the same hazard as other major operations performed upon patients with arteriosclerosis due to advanced age or to diabetes mellitus. Of the 6 deaths which occurred in the series of 50 amputations, 3 were probably contributed to by errors in surgical judgment.

Type of operation. Except for 1 upper leg amputation, all operations were performed at the supracondylar or midthigh level. Only 1 major reamputation was necessary (Case 1). No guillotine operation was performed. In the presence of advanced organic arterial occlusion there should be no compromising on the level for amputation. Two of the deaths followed major amputations which were resorted to after less radical surgery had failed to give relief. Depending upon the surgeon's judgment, wound nonclosure or closure was used, with or without drainage.

Surgical and medical care. The surgery was performed by 14 members of the surgical staff. One hospital death occurred on 6 surgical services. The medical care was provided by various members of the medical staff. Diabetic management is largely standardized by the diabetic service which may be said to account for the excellent convalescence of the diabetic patients and for the absence of deaths from diabetic coma or from wound infection (series I).

Anesthesia. With 2 exceptions all major operations were performed under ethylene anesthesia. The 2 patients mentioned were operated upon under local infiltrating and block anesthesia.

CASE REPORTS OF HOSPITAL DEATHS

Senile arteriosclerosis

CASE 1. Mr. C. C., aged 79 years, was admitted March 28, 1935, suffering with gangrene of left first toe. Oscillometric readings revealed complete organic arterial occlusion at the ankle. He remained in the hospital 17 days. Fifty hours of pavaex treatments were given and the condition of the toe and foot improved. On April 19, 1935, he was readmitted to the hospital for acute urinary retention for which electroresection of the prostate was performed. He was discharged from the hospital May 19, 1935.

He was readmitted to the hospital July 10, 1935, with recurrence of pain and gangrene of the toe of 1 month's duration. On July 13, 1935, the toe was amputated and because of the absence of bleeding, midleg amputation was then performed. The midleg stump failed to heal and on September 5, 1935, a midthigh amputation was performed. Infection of the gangrenous stump continued until death from bronchopneumonia occurred on October 12, 1935.

CASE 2. Mr. O. T., aged 80 years, was admitted September 21, 1936, for infected gangrene of the left first toe and foot. Because of the advanced arterial occlusion and infection of the foot which had been present for 3 months prior to examination, midthigh amputation was advised and performed the day following admission. Right pulmonary atelectasis followed operation and the patient died on the 12th postoperative day from bronchopneumonia.

CASE 3. Mr. A. M., aged 73 years, had been in ill health for more than 10 years and suffered with circulatory symptoms of the lower extremities for 8 years prior to his admission October 3, 1939. Daily treatments of alternating negative pressure but no positive pressure were given for 7 days when an extension of the infection was noted with mouth temperature of 100 degrees F.

Midthigh amputation was then performed. The wound was closed without drainage as is recommended in some reports in the literature. In this instance, however, because of the infection present, the surgical decision to close the wound without drainage was illadvised.

The day following amputation the patient's temperature rose from 100 to 102 degrees F. and his condition became progressively worse. The next day the sutures were removed and a large amount of old clotted blood was evacuated. Bacteriological studies revealed mixed infection with anaerobes, probably Bacillus welchii (milk fermentation not typical). He died on the 3d postoperative day from gas bacillus infection (Bacillus welchii) of the amputation stump, thigh, abdominal wall, scrotum, left psoas muscle, and mesentery of the small bowel.

CASE 4. Mr. J. E., aged 80 years, was admitted September 9, 1940, suffering with gangrene of the left 4th and 5th toes and advanced organic arterial disease. Oscillometric readings revealed complete occlusion of the main arteries at the knee. Although the toes appeared infected, only an occasional mouth temperature of 99 degrees F. was recorded. Twenty-one hours of treatment with alternating negative pressure but no positive pressure were cautiously given, but the condition failed to improve and the 2 toes became more involved in the gangrenous process. Despite the evidence of infection, amputation of the 4th and 5th toes was performed under local infiltrating anesthesia. The mouth temperature almost immediately became elevated to 102 degrees F. The infection spread rapidly, and the pain increased.

Four days after the toes were amputated, midthigh amputation was performed under local anesthesia. The wound was closed without drainage. The stump rapidly became gangrenous and infected, and the mouth temperature remained elevated. The patient's general condition became progressively worse, and he died on the 32d postoperative day from a cerebral accident.

Three of the 4 deaths followed serious infection of the operative wound. Two of these had initial minor amputations through areas of infected gangrene of the toes although neither had a febrile course. The third death followed gas gangrene infection in which case a large hematoma was evacuated the 2d day after closure of the wound without drainage. These observations emphasize the danger of local amputations in the presence of advanced organic arterial disease and of nondrainage of wounds following amputation for infected gangrene.

Diabetic arteriosclerosis

CASE 5. Mrs. S., aged 61 years, was admitted October 12, 1935, suffering with advanced bilateral diabetic vascular disease. Oscillometric readings revealed complete occlusion of the femoral arteries. She remained in the hospital for 6 days during which time large painful infarcts of both heels failed to respond to pavaex treatments. The patient was readmitted January 2, 1936. Left midthigh amputation was performed February 14, 1936, with recovery and discharge from the hospital on March 13, 1936.

On September 10, 1936, she resumed pavaex treatments because of continuous pain in the right leg and foot. Complete relief from pain occurred during treatment. There was no infection present. Because of her inability to continue treatments she requested the second midthigh amputation. This was performed September 29, 1936. Sudden death from pulmonary embolism occurred October 3, 1936.

CASE 6. Mr. G., aged 58 years, was admitted January 9, 1936, suffering with bilateral diabetic vascular disease. Thirteen hours of pavaex treatment were given. Because of the continuous rest pain in the right foot, supracondylar amputation was performed January 16, 1936. He was discharged from the hospital February 2, 1936, and returned

April 17, 1936, for periodic pavaex treatments of the left leg until March, 1937. Marked improvement in the condition of the leg and foot followed the treatments.

Sixteen months later, on July 31, 1938, he returned to the hospital with recurrence of pain in the left foot. Nine months previously he had been confined to bed for 6 weeks with cardiac decompensation. On admission the first toe was red and inflamed. No pavaex treatments were given because of spreading gangrene and severe diabetes. Midthigh amputation was performed August 16, 1938. Cardiac decompensation and pulmonary edema followed operation and the patient died August 20, 1938.

Neither of the 2 deaths following the second major amputation for diabetic gangrene can be attributed to delay in operating because of attempts to save the limb by conservative treatment. Both individuals were suffering with far advanced arteriosclerosis and had previously undergone successful major amputation of the other extremity.

EVALUATION

Major amputation for advanced arterial disease is definitely indicated when a limb cannot be saved by conservative treatment or when the life of the patient is endangered by serious complications. In the 50 amputations (series I) under the advisement of the vascular therapy department the mortality rate of 12 per cent is especially favorable in view of the extensive use of conservative treatment and the fact that the operations were performed on 14 surgical services. During the same period 29 extremities which were not seen in the department were amputated with a mortality rate of 20.7 per cent. These results do not confirm the contention of de Takats and Reynolds, Veal, and others (1), that operative delay due to conservative treatment contributes to the mortality rate from amputations.

Although the series herewith reported is not as large as those reported elsewhere, the 50 amputations occurred in a series of 226 extremities with main artery occlusion. Despite the fact that amputations were delayed and the operations were not performed by a special surgical service, the hospital mortality in the various classifications of advanced arterial disease compares very favorably with the reports from specialized services elsewhere. Williams and O'Kane were able to reduce their mortality rate from 85 per cent in 1931 to 36 per cent in 1935 after amputation cases were concentrated on one surgical and one medical service. McKittrick's series (5, 6, 7) of 496 amputations had a mortality rate of 14 per cent and Veal's series of 171 amputations had a mortality rate of 39.1 per cent. From the University of Pennsylvania Hospital, Eliason reported 83 major amputations with a 25 per cent mortality rate from amputation for diabetic gangrene. These mortality rates are higher than should be expected on specialized services with large series.

In order to lower the mortality rate from amputation it is advisable to study the causes of the operative deaths. More emphasis should be placed on the surgical judgment that is used in the individual case than on the number of amputation cases. Three of the 6 deaths herewith reported were probably contributed to by errors in surgical judgment as when minor amputations preceded major amputation and nondrainage of a closed wound resulted in serious infections of the stumps. Experienced surgical judgment is especially needed in deciding upon wound closure or nonclosure and drainage or nondrainage. McKittrick with his extensive experience advises either a guillotine operation for infected gangrene or wound closure without drainage while Eliason recommends closure with drainage. Faxon and Taylor (9, 10) both advise against draining for primary closed amputations. It is not possible for the less experienced surgeon to appraise individual cases. In the series reported the largest number on one surgical service was 17 major amputations with 1 death (mortality, 5.5 per cent); nonclosure or closure with a small gutta-percha drain was used for a few days in almost all the cases. In general, it is safer when major amputation is done for infected gangrene that the operative wound be drained for a few days to assure evacuation of blood or primary wound secretion.

The actual age of the patient should not be an important contraindication for major amputation. Because of the advanced age of some patients there is a risk in operating, but the risk is greater when amputation is not done to relieve unnecessary suffering or to

save the life of the patient. The operative risk of this operation should not be greater than that for other major operations upon patients of advanced age.

CONCLUSIONS

Operative delay due to efforts to save the limb by nonoperative treatment did not contribute to the mortality in the 50 major amputations for advanced arterial disease herein discussed. Despite the extensive use of conservative treatment the mortality rate in these cases is the lowest thus far recorded.

In the presence of extensive organic arterial occlusion, minor amputations are usually unsuccessful and increase the risk incurred in secondary major amputation.

Nondrainage of closed amputation wounds may prove dangerous and is especially ill-advised when there is a possibility of gas bacillus infection.

The operative risk involved in major amputation should not be greater than that for other major operations performed upon patients of advanced age with extensive arteriosclerosis.

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A METHOD FOR OBTAINING VENOGRAMS OF THE VEINS OF THE EXTREMITIES

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ROENTGENOGRAPHIC visualization of the veins of the extremities by contrast media is becoming increasingly popular both for the study of relatively recent thrombosis in order to disclose its presence and location, and for the study of long standing occlusion of the deep venous system. This article will not discuss the value of venography, but will outline a simple method of performing it.

Bauer and later Dougherty and Homans described the commonly used method of injecting contrast media into the veins of the lower extremity. Their method consisted of cannulating the external saphenous vein after it had been exposed by incision under local anesthesia. Because the external saphenous vein is very deep seated, it is not feasible to insert a needle into it without incision and exposure. The method I propose and find satisfactory differs from theirs chiefly in obviating the cutting down operation. It is performed thus:

1. The patient sits on the x-ray table on which the plate is to be made.

2. With the legs dependent a 20 gauge needle is inserted into a vein on the dorsum of the foot or on the ankle, one of the tributaries of the internal saphenous system. The course of the internal saphenous is anterior to the internal malleolus and it is relatively superficial, usually permitting the insertion of a needle without an incision.

3. The tubing of an infusion set containing normal salt solution is connected with the needle. The infusion is permitted to drip relatively rapidly.

4. The needle is then strapped securely in position with adhesive, and the patient rotates and lies down on the table.

5. A large casette containing the films is placed behind the calf and thigh (Fig. 1). The leg is slightly externally rotated.

6. A gum rubber tourniquet is applied around the leg, usually at the junction of the middle and lower thirds, sufficiently tight to impede circulation in the superficial veins. This serves to shunt the infusion from the superficial into the deep system.

7. A 20 cubic centimeter syringe is used to remove the diodrast from its vaccine capped ampul. The 20 cubic centimeters of diodrast (35 per cent) is slowly injected into the tubing of the infusion just above the needle.

8. Five seconds after diodrast is completely delivered, the technician makes the exposure.

9. After the exposure the infusion continues to run for 200 cubic centimeters in order to wash the diodrast from the veins.

It is then possible to rotate the leg and get a lateral or oblique view after the plate is replaced with a new one, or, if it is desired, a new plate may be placed higher under the thigh and the femoral veins exposed.

Accurate visualization of the deep veins may be obtained by this method as is demonstrated in the accompanying roentgenograms.

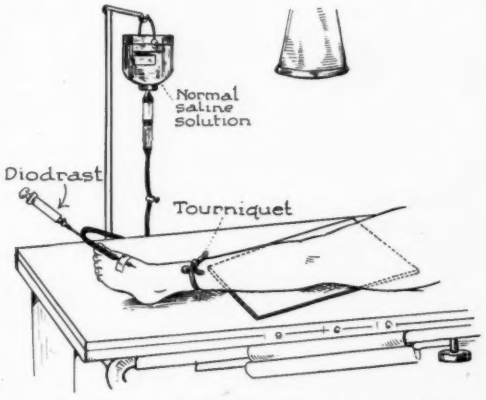

Fig. 1. Diagram illustrating the method of shunting contrast media from superficial into the deep venous system by use of a tourniquet around the leg. The steps in the procedure are described in the text.

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Fig. 2. Fig. 3. Fig. 4. Fig. 5.

Fig. 2. Anteroposterior and lateral venograms in leg in which the internal saphenous system was obstructed by recent thrombosis near the knee (see arrow). The infusion was running into superficial vein of the foot, a tributary of the internal saphenous system. No tourniquet was used. The diodrast is seen in the saphenous up to the point of thrombosis as is indicated by the arrow. The diodrast is also shunted into the deep system which is filled and found to be normal. *A.P.T.*, indicate anterior and posterior tibials.

Fig. 3. Venogram showing failure to disclose any of the deep veins when tourniquet was placed around thigh just above knee and contrast media was injected into superficial vein of foot. The diodrast in this instance was not shunted into the deep system. *I.S.*, Internal saphenous.

Fig. 4. Anteroposterior and lateral roentgenograms of the leg. The veins are visualized by diodrast. A needle was inserted into a vein on the dorsum of the foot, and a tourniquet, arrow, around the junction of the middle and lower thirds of the leg shunted the blood into the deep system. The venous system is adequately exposed showing posterior tibial and anterior tibial veins and their juncture above the interosseous membrane to form the popliteal. Several valves are disclosed. The venous system looks normal. *E.S.*, External saphenous. Compare this roentgenogram with the blocked deep system on the opposite leg of the same patient shown in Figure 5.

Fig. 5. The left leg of the patient whose right leg is shown in Figure 4, had long standing edema from obstruction of the deep venous system. This resulted from a fracture of the femur 6 years ago. The arrow indicates the tourniquet which was applied at the junction of the middle and lower thirds of the leg. Diodrast may be seen in the superficial system below and above the tourniquet and in some veins of the deep system below it. Although it has forced its way up the superficial system and may be seen in the internal saphenous vein, *I. S.*, of the thigh, none of the deep veins are visualized. A control venogram of the right leg (Fig. 4) which was normal showed visualization of the deep veins under the same circumstances. The tourniquet applied at the juncture of the middle and lower thirds of the leg shunted the contrast media into the deep system. *A.T.*, Anterior tibial.

I have attempted to obtain venograms of the deep system by injecting diodrast into the superficial veins of the foot without the use of the tourniquet to shunt the media into the deep system. This, however, has not been uniformly successful because the diodrast usually goes up the superficial system and does not always expose the deep system. Moreover, if the tourniquet is placed high around the thigh, the contrast media is not promptly shunted into the deep system and the deep veins will not be visualized.

Though the superficial system may not be exposed well by this particular method, superficial thromboses are usually evident on clinical examination.

Finally, a word of caution should be expressed concerning venography. More extensive thrombosis (4) and even death (3) have been reported as complications.

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THE CARBON DIOXIDE SNOW-ELECTROCAUTERY TECHNIQUE FOR OCCLUSION OF LARGE VEINS

Suggested Application to Venous Angioma of the Brain

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A NEW technique for the occlusion of large venous channels, for use when conventional methods are not adequate, has been developed. The details of this procedure, and its possible application in neurosurgery, will be considered.

This work was begun in the hope of finding an effective treatment for venous angioma of the brain, which is thought to be a congenital blood vessel malformation rather than a new-growth. There are simple, serpentine, and racemose types. The simple type consists of a hugely dilated single vein, the serpentine of a group of enlarged vessels lying superficially, and the racemose of a mass of distended veins which lies on the surface and extends deeply into the substance of the brain replacing nervous tissue. On the surface the serpentine and racemose types look much alike and cannot be distinguished. Angiomatous vessels are very thin walled and fragile. Occasionally, thick but brittle walls are seen as the result of hyaline change.

Treatment has included surgery and x-ray therapy. The principal danger in the surgical approach to this lesion is severe bleeding from extremely large and fragile vessels, at times uncontrollable. The ligature and the electrocautery have been used with very little success. At operation these lesions, for the most part, have been simply exposed without attempt at removal or obliteration. This occurred in the cases presented by Spiller, Dandy, and Brock and Dyke. Others have attempted removal with severe, and sometimes fatal, hemorrhage resulting, as reported by v. Bergmann, Krause, Worster-Drought and Ballance, Perthes, and Cushing and Bailey. Radiation therapy has also been attempted on these vascular masses, but the results have not been encouraging.

Various ways of obliterating large vessels were therefore considered, and finally an effective technique was developed, which involves the combined use of carbon dioxide snow and the electrocautery. Application of the electrocautery alone to a large vein almost always results in a tear. The heat produced is not sufficient to coagulate the vessel walls and the blood stream; the major effect of the cautery is then exerted on the proximal wall, which tears. Therefore, temporary emptying of the vessel, eliminating the interposed blood stream, would be desirable to permit coagulation of the apposed walls. Carbon dioxide snow applied with moderate pressure empties the lumen, by forcing the blood out of the strip, and freezes the vessel; the electrocautery may then be applied and the vein occluded. This procedure may perhaps be of use in the treatment of venous angioma of the brain.

EQUIPMENT

Carbon dioxide snow, or dry ice, is a widely used refrigerant, which has a temperature of −78 degrees C. It is easily obtained from distributors of dry ice and ice cream, and may be kept in vacuum jars, in which there is a loss of 5 per cent per day. A film of gas surrounds the material, acting as an insulator, and must be removed by pressure before freezing can take place. Pressure of carbon dioxide snow against tissues causes immediate freezing of the area in direct contact with it. The rate and depth of freezing depend upon the pressure exerted; conduction of heat from below extends the freezing to greater depths.

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Dry ice is bacteriologically sterile. Repeated efforts to grow organisms on agar, blood agar, broth, and anaerobic meat broth culture have failed.

It can be cut into desired shapes with a hack saw. A block of the freezing agent is placed into a wooden frame with slots at intervals to guide the saw. There is an overlapping border on the sides, by means of which the device is clamped to a table. The cut pieces in these experiments measured 6 by 2 by 2 centimeters. Smaller sections are best cut with a hammer and moderately keen edged knife.

A curved clamp was found best for grasping and applying the carbon dioxide snow. When dry ice is held in a steel instrument, the metal becomes cold and condensed water vapor, which immediately freezes, is deposited on the prongs. This frost causes the instrument to adhere to moist gauze and tissues. To prevent this, the prongs of the instrument are covered with close fitting rubber tubing.

Both spark-gap and vacuum tube electrocauteries were employed in these experiments. The spark-gap machine was the Liebel-Flarsheim portable Bovie electrosurgical unit, which operates at approximately 800,000 cycles per second and has a wave train frequency of 7,000 per second. The vacuum tube apparatus was the Cameron cauteradio model O, a small portable machine, which operates at 5,000,000 oscillations per second. The ball electrode measuring 5 millimeters in diameter was used on the vessels.

TECHNIQUE

This procedure has been used successfully on the inferior vena cava of cats between the renal and iliac vessels in more than 50 experiments. The vessel, of an average diameter of 6 millimeters, was exposed by a lower abdominal midline incision, retraction cephalad of the small bowel, and dissection through the peritoneum.

When a block of dry ice is applied to a segment of blood vessel with moderate pressure for one minute and then removed, the vessel is seen to be covered with frost. It contains no blood and is cold and hard on palpation. At the end of about one minute, blood appears at each end of the frozen strip. The two columns slowly move toward the middle where they join, and normal blood flow is resumed. The vessel, being undamaged, then appears exactly as it did before freezing. Pressure is an important factor both in emptying and freezing a vascular channel. Application of carbon dioxide snow without pressure leaves the vessel unfrozen with blood in the lumen.

To occlude a segment of vein, a block of dry ice is applied to it with moderate pressure; this also freezes lateral tributaries for a short distance before they enter the vessel. A larger strip is frozen than is to be coagulated, for example, freezing 6 centimeters and coagulating the middle 3 centimeters. After one minute the refrigerant is removed and the electrocautery is applied. The frozen extremities and tributaries are watched. If blood enters them, electrocoagulation is stopped, and the procedure is repeated.

So long as the extremities and the lateral tributaries are frozen, the strip usually remains flat and bloodless during coagulation. If, however, blood appears in the lumen, coagulation is stopped. The ends are thawed, and the procedure is repeated.

The presence of blood in the frozen strip may be accounted for in a number of ways: (1) The vessel may have been incompletely emptied because of insufficient pressure in the application of the refrigerant. (2) The blood may have entered through deep tributaries. The presence of very small quantities of blood does not offer much hindrance to effective coagulation. Deep tributaries in these experiments have caused no difficulty. If the deep tributaries of a vein were very large, it might be possible gradually to occlude the vessel by repeating the procedure several times, stopping when blood appeared in the lumen.

In coagulation, the objective is occlusion with a minimum of damage to the vessel wall. Although it would be best to obliterate the lumen with no carbonization of tissue, low intensities of current frequently coagulate only a part of the wall without occlusion. Therefore, a current of moderate strength has been used, resulting in slight carbonization of the anterior wall. It is difficult to know exactly how much current is delivered at each

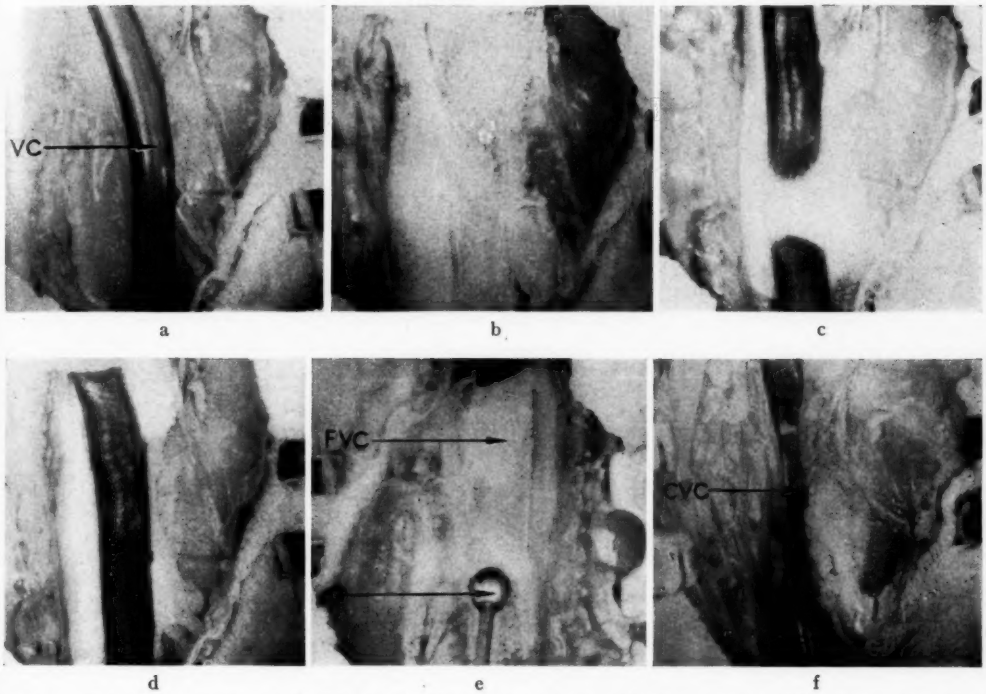
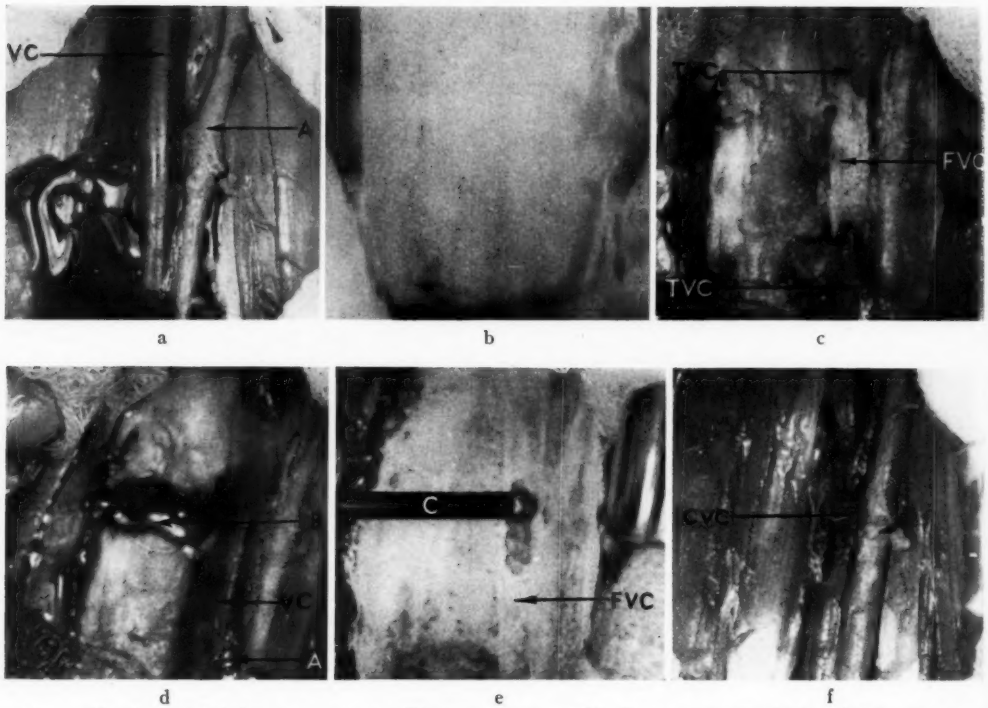


Fig. 1. Cat inferior vena cava, 6 millimeters in diameter, which was frozen and thawed; and then frozen again and electrocoagulated. a, Normal. *VC*, Inferior vena cava. b, Frozen. c, Thawing. d, Thawed. e, Application of electrocautery to refrozen vessel. *FVC*, Frozen segment of the inferior vena cava. *C*, Electrocautery. f, Coagulated. *CVC*, indicates the coagulated segment of the inferior vena cava.

setting of the current control. In these experiments the control has been set at 2.5 in the vacuum tube machine and at 30–35 in the spark-gap electrocautery. The ball electrode is moved rapidly back and forth over the center of the frozen strip, in order to cover the area and to distribute the current uniformly. The procedure is continued until coagulation and a slight degree of carbonization of tissue have occurred. At this point, the vessel is usually occluded. The frozen ends are then allowed to thaw. If the lumen is not completely obliterated, the vessel is refrozen and again coagulated. To occlude additional strips, the procedure is repeated.

After one segment has been occluded, the portion of the vessel proximal to it is even more easily emptied by freezing with moderate pressure (allowing the dry ice to overlap a short distance on the coagulated portion) as the main source of supply has been cut off and blood is being moved in the direction of flow. Slightly more difficulty may be encountered in emptying strips distal to the coagulated segment, because blood is being moved against the venous current. Nevertheless, it is almost always accomplished by the application of dry ice with pressure in the usual manner; allowing the refrigerant to overlap slightly on the occluded strip is of help. If this is not effective, one end of the block of carbon dioxide snow is placed on the near part of the coagulated segment. The piece is then lowered until its whole undersurface is in contact with the vessel. Pressure is applied as it is moved into position. By these methods, additional portions of the vessel may be emptied and then coagulated.

If cauterization is carried too far or is continued in spite of the presence of blood in the



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d e f

Fig. 2. Bleeding cat inferior vena cava, 6 millimeters in diameter, frozen, and thawed to demonstrate site of tear; and then frozen and coagulated. a, Bleeding. *VC*, Inferior vena cava. *A*, Abdominal aorta. b, Frozen. c, Thawing. *TVC*, Thawed segment of the inferior vena cava. *FVC*, Frozen segment of the inferior vena cava. d, Thawed, with blood oozing from tear. *B*, Oozing blood. e, Application of electrocautery to refrozen vessel. *C*, Electrocautery. f, Coagulated. *CVC*, Coagulated segment of the inferior vena cava.

lumen, the vessel may tear. In that event, the strip is refrozen and the area about the tear is coagulated. When the location of the tear is not known, the vessel is frozen for 15 seconds, and then allowed to thaw until blood oozes from the opening. When the laceration has been identified, the segment about it is then refrozen in the usual manner and coagulated. Free blood is frozen by the dry ice and, unless excessive, does not interfere with the procedure. If much blood is present, it may be removed by suction while the dry ice is in place. This procedure has been used more than twenty times on the purposely torn inferior vena cava of cats, without failure.

In short, to occlude a segment of vein, a block of carbon dioxide snow is applied to it with moderate pressure. After one minute the refrigerant is removed. The electrocautery is passed back and forth over the vessel, until coagulation and a slight degree of carbonization have occurred.

In order successfully to occlude venous channels, or permanently control bleeding from them by the use of the carbon dioxide snow-electrocautery technique, the vessels must be emptied of blood. The procedure may therefore be used only on veins in their long axes. When only the cross-section of a blood vessel presents itself, as may be the case after excision of a block of cortical tissue, bleeding cannot be permanently controlled in this manner.

The widest vessel occluded by use of this technique was a dog inferior vena cava, 13 millimeters in diameter. In so far as length is concerned, a vein of any extent may be obliterated by freezing and coagulating con-

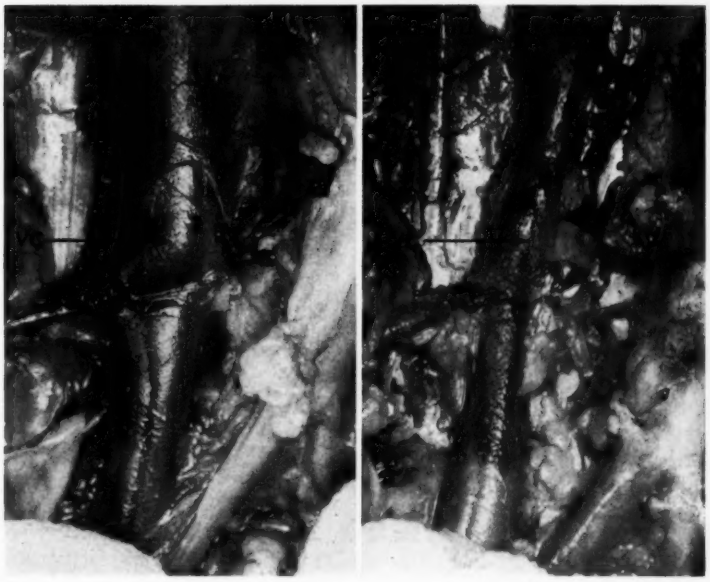

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Fig. 3. Dog inferior vena cava, 13 millimeters in diameter, frozen and coagulated. a, Normal. *VC*, Inferior vena cava. b, Coagulated. *CVC*, Coagulated segment of the inferior vena cava.

secutive strips. Work is in progress to develop a similar technique for the occlusion of arteries, for possible use in the treatment of arteriovenous angioma of the brain.

CONSIDERATION OF LOW TEMPERATURE FREEZING

In 1938 Jahnel reported his work on the freezing of spermatozoa at extremely low temperatures. Specimens were maintained at −196 degrees C. in liquid nitrogen for 52 hours. On thawing, a considerable number of normal, motile cells was seen. Another specimen was kept at −79 degrees C. in a mixture of carbon dioxide snow and alcohol for 40 days, with the same result. Surprisingly, at temperatures nearer the freezing point of water, −10 degrees C. and −20 degrees C., very few normal cells were visible on thawing.

Several theories have been advanced to explain why freezing at very low temperatures does so little damage to cells as compared to that done by freezing at temperatures just below 0 degrees C. Richardson and Scherubel studied cells under the microscope during freezing and observed that at temperatures just below the freezing point of water, ice formed in the extracellular spaces sooner than it did intracellularly, and water was extracted from the cell. Damage may result from the mechanical compression of the cell, or from an increased concentration of toxic substances within it. Plank, Ehrenbaum, and Reuter demonstrated that the rate of freezing was important, since, in tissues frozen quickly at very low temperatures, ice formed within and without the cells simultaneously without the passage of water. Mechanical compression and increased concentration of toxic substances are both avoided.

A somewhat different explanation is offered by the researches of Moran and Hardy. Working with colloids they showed that, in slow freezing, crystallization progressed from few centers with the formation of large crystals which distorted the normal architecture of the colloid. In rapid freezing, crystallization proceeded from many centers, the crys-

tals were much smaller and the structure of the colloid was preserved.

These theories offer possible explanations of why low temperature freezing does little damage at the time of refrigeration. Maintenance in a frozen state for long periods of time without injury probably depends on the cessation or diminution of metabolic activity. If cell material is not consumed at all or is expended only in small quantities, there is little need for elimination or replenishment. This phase of the problem has not as yet been completely worked out.

Jahnel's findings on the low temperature freezing of spermatozoa have been duplicated in living brain tissue. Koskoff and associates have reported a method of removing blocks of brain tissue after *in situ* refrigeration with liquid nitrogen, which has a temperature of —196 degrees C. An instrument which they have devised is inserted into the brain. Liquid nitrogen is then poured into it and after 1 minute a core of frozen tissue is delivered. Microscopic examination of the excised block revealed normal cortical architecture. Study of the area adjacent to the crater disclosed small hemorrhages but intact cell structure. These findings indicate that freezing at very low temperatures does not injure brain tissue.

It is of interest that other investigators, including Astapow and Bobkow, Speransky, and Nims and associates, have reported considerable damage following freezing of the brains of experimental animals. The freezing agents used were carbon dioxide gas and a mixture of carbon dioxide snow and ether; these were applied, not directly, but in metal containers. Very cold metal surfaces adhere to moist tissues and are separated with much difficulty, whereas blocks of dry ice are easily removed. In the instrument devised for refrigeration with carbon dioxide gas, the gas is transmitted through a tube into a metal chamber which is applied to the cortex. Fedoroff, in describing the removal of the apparatus from the frozen cortex, has said, "Particular difficulties are found in the 'dosage' of the freezing, as the freezing apparatus can not be separated from the hard surface of the brain after thawing. The dura and the brain are usually torn during the removal. It can be successfully separated by striking extremely sharp blows on one or more surfaces of the tube of the instrument." It seems not unlikely that mechanical trauma has played a considerable part in the damage resulting from this type of refrigeration.

There is also an element of mechanical trauma, though considerably less, in freezing with blocks of dry ice, as the refrigerant must be applied with moderate pressure for the reasons mentioned. Therefore, in evaluating the pathological effects of freezing with blocks of dry ice, the part played by pressure must be considered.

A 1 centimeter strip of the inferior vena cava of a cat was frozen with a block of carbon dioxide snow applied with moderate pressure for 1 minute, in order to study the results of low temperature freezing of vascular tissue. Examination 3 weeks later disclosed that the vessel was patent and that there was no sterile abscess or infection. Microscopic examination showed the vessel to be of normal appearance. A slight separation of the fibers of the outer layer of the adventitia was the only change seen. These findings might have been expected from what is known of low temperature freezing, and indicate that vascular tissue can tolerate the pressure necessary to empty and freeze a blood vessel.

In order to study the effects of freezing brain tissue with blocks of carbon dioxide snow, the brains of 5 cats were exposed and dry ice was applied with moderate pressure. The freezing agent was placed on an area of cortex behind the motor strip for 1 minute. Pressure was tolerated with very little displacement of brain tissue. No change in vital signs was noted during the period of freezing, nor did convulsive movements appear. After the dry ice was removed, a frost was seen over the frozen area, which thawed within 1 minute. The thawed surface had a faintly blue tinge and the vessels were dilated; surrounding areas showed no change. The motor strip was frozen in the same manner without convulsions. To have some idea of the damage caused by pressure alone, a piece of plastic material of the same size as the block of dry ice was placed with moderate pressure on a similar area of cortex in a cat for the same

length of time. The animals were observed for 3 weeks during which they seemed normal. The frozen areas were then re-exposed. No evidence of sterile abscess or infection was found. A grayish-yellow discoloration was visible at the site of freezing, but the adjacent area was normal in appearance. On cross-section the discoloration was visible to a depth of 1 millimeter, below which the tissues seemed unchanged.

Study of the microscopic sections showed that in all specimens by far the greater part of the frozen area was entirely normal with complete preservation of cortical architecture. Damage was limited to a small portion of the frozen surface and in those areas it varied in depth between fractions of 1 and 1.5 millimeters. In some cases pathological changes were restricted to the upper layers of the cortex, whereas in others the entire cortex was destroyed. Damage did not extend below the cortex which, in these areas of the cat's brain, is between 1 and 1.5 millimeters in depth. When the damage was superficial, the injured area showed disorganization of the zonal layer with many fat granule cells. Nerve cells had partly or completely disappeared and some of those remaining were sclerosed and exhibited tortuous dendrites. Glia cells replaced damaged parenchyma. In some sections vessels were injected and occasional hemorrhage and round cell infiltration were noted. In cases of deeper damage, the cortex was no longer visible but the white matter at these points was normal.

Microscopic examination of the area of cortex to which pressure had been applied without freezing revealed a pathological picture almost identical with that described for the frozen brain. The greater portion of the section was normal with complete preservation of cortical structure. Damage was limited to a small part which showed almost complete destruction of the cortex with replacement of nerve cells by glia. There was also some damage to the white matter beneath the cortex, where many fat granule cells were seen.

At this point an attempt will be made to integrate the material that has been presented. The temperature of dry ice, —78 degrees C., is low enough to provide rapid freezing of tissues without damage, as has been shown by Jahnel's work with spermatozoa and my own experiences in freezing the inferior vena cava of the cat. That brain tissue will tolerate low temperature freezing without damage has been demonstrated by the work of Koskoff and his associates with liquid nitrogen. Dry ice freezing differs from that with liquid nitrogen, in that pressure is required. The application of pressure alone without freezing has been shown to cause cortical damage almost identical with that resulting from dry ice freezing. It therefore seems likely that damage to the cortex following freezing with carbon dioxide snow is due not to refrigeration but to pressure.

Application of the carbon dioxide snow-electrocautery technique to the occlusion of blood vessels of the human brain should cause little cortical damage. First of all, both freezing and coagulation are to be done on the blood vessel wall and not on the cortex. Second, if, by chance, adjacent cortex is frozen during the procedure, the injury can be but slight. For, in the experimental animal only a small part of the frozen surface was damaged, and that to a depth varying between fractions of 1 and 1.5 millimeters. In the human cortex, the greatest depth of which is 4 millimeters in the motor area, such damage should in most instances be superficial and negligible.

PATHOLOGY OF VESSEL THREE WEEKS AFTER FREEZING AND COAGULATION[1]

In order to study the long term effects of freezing and coagulating a vein, a 1 centimeter strip of the inferior vena cava of a cat was occluded. Of particular interest were the questions of permanence of closure and pathology. Three weeks after operation, the segment was found to be still occluded with many adhesions to surrounding tissues. Rupture or canalization had not occurred, and there was no evidence of sterile abscess or infection. The vessel was much shrunken and the very small lumen was completely filled with a black coagulum. Microscopic study showed that the coagulum was composed of coagulated red cells and blood pigment. The greater part

[1]Drs. Abner Wolf and David Cowen were of great assistance in evaluating the pathological results.

of the wall had a hyaline appearance as a result of coagulation.

SUMMARY

A new method for the occlusion of, and the control of bleeding from, large venous channels in their long axes through the combined use of carbon dioxide snow and the electrocautery has been developed. The resulting closure is permanent. The procedure is such as to do little damage to adjacent brain tissue. Application of this technique to the treatment of venous angioma of the brain has been suggested.

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COMPLICATIONS AND CAUSES OF MORTALITY OF THE SURGICAL TREATMENT OF CARCINOMA OF THE COLON AND RECTUM

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SINCE July, 1937, practically all of the small and large bowel material at the Mt. Sinai Hospital has been assigned to this surgical service. As a result, an unusual opportunity was afforded a small group of surgeons to carry out a concentrated study of a fairly large group of patients. It is the purpose of this communication to report our experiences to date, especially stressing the complications with which we have had to contend, the methods adopted to obviate them, and the causes of operative fatalities.

It is important to stress that many of the patients admitted to the wards of the Mt. Sinai Hospital do not represent the best physical material for major surgical procedures. Serious cardiovascular disease is common, as are diabetes and kidney disease. Many of the patients have led sedentary lives with little physical exercise, with the result that muscle tone is poor and the speed of recuperation is greatly reduced. Nutritional disturbances are common, and there is great susceptibility to pulmonary infections. We are convinced that these factors are of considerable importance in influencing the mortality of major abdominal surgery in a large group of cases. There is a great difference in the physical status of ward patients living in large urban centers and those coming from rural communities. We do not believe that this has been stressed sufficiently in the past and that it may be an important reason for the disparity in the operative mortality statistics reported from various sections of the country.

We therefore formulated a plan of preoperative preparation, surgical procedure, and postoperative care which took cognizance of the necessity of overcoming or lessening the associated disabilities with which we were often primarily confronted. The preoperative period of preparation was frequently prolonged for 2 or 3 weeks to overcome anemia, nutritional and vitamin disturbances, and to treat kidney complications and cardiovascular disabilities. Operative procedures were more often staged than not. We believe that the staging of operations for carcinoma of the colon has been the most important contribution to surgery of the colon in recent years. Finally, great care has been given to the details of postoperative care. This was found to be equal in importance to the preoperative period of rehabilitation.

Under this plan, it soon became evident that our incidence of operability rapidly increased. It seems worth while to enlarge on this aspect of the subject. Operability and mortality, of necessity, are closely related. Factors which influence operability have a direct bearing on mortality. A large country-wide experience has shown that, by extending the scope of operability, the mortality rate increased, but with a proportionate increase in the number of patients surviving the 5 and 10 year periods. These facts have influenced us in accepting patients for radical surgery who might otherwise have been rejected for fear of an increased operative mortality. Except in rare instances and under unusual circumstances, our index of operability has not been influenced by such considerations as age of the patient, obesity, loss of weight, anemia, or associated chronic diseases. However, we are particularly wary of the patient who has had a recent coronary thrombosis. It has been our experience that these patients take radical abdominal surgery very poorly. It seems wise

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to defer operation in such cases until cardiac reserve has been greatly restored. In general, it may be said that our index of operability has been influenced much more by conditions associated with the growth *per se*, such as situation of the tumor, fixation to adjacent structures (removable or otherwise), extent of lymph node involvement, perforation and hepatic metastases. Fixation to neighboring vital structures naturally makes for inoperability, but on a number of occasions it was possible to remove a section of bladder wall, a loop of small intestine, the entire uterus, the posterior vaginal wall, or a section of the abdominal wall, which had become infiltrated by an adherent neoplasm. Curiously enough, these patients have done unusually well.

The extent of lymph node involvement influences operability to a great degree and the decision to undertake radical surgery will rest, first, on the accuracy of the interpretation of the cause of the node enlargement (neoplastic or inflammatory), and second, on the experience and boldness of the surgeon. The finding of liver metastases at the time of exploration renders the situation hopeless from the standpoint of cure. However, with the knowledge that patients with hepatic involvement frequently survive for 2 or 3 years, it is occasionally justifiable to resect a small movable tumor of the left colon causing obstruction or to perform an ileotransverse colostomy to short-circuit a large infected neoplasm of the right colon. We doubt that it is ever justifiable to perform an abdominoperineal resection for cancer of the rectum with associated liver metastases.

Free perforation of a colonic neoplasm still constitutes a fairly lethal complication, in spite of sulfonamide therapy. However, a walled-off perforation with pericolonic abscess, most commonly encountered in the cecum and sigmoid, has not been a definite contraindication to radical surgery, provided the principles of preliminary diversion of the fecal stream and extensive drainage are adhered to.

PREOPERATIVE PREPARATION

It is not our purpose to describe in detail the methods utilized to rehabilitate these patients before operation. Only general principles will be mentioned. Extending this period of preparation to 1, 2, or more weeks is time very well spent. It usually pays large dividends. The diet is usually of the low residue, high caloric variety. Cleansing of the bowel is accomplished by mild purgation and colonic irrigations. With obstructing neoplasms, more and more use has been made of the Miller-Abbott tube, as already reported by Klein of this service. In fact, in nonobstructing tumors when a suture anastomosis is contemplated, the Miller-Abbott tube is passed before operation and maintained for 5 or 6 days thereafter. However, while the employment of the tube makes for a smoother convalescence, its use must be watched with care because complications due to its very presence may occur. We might mention perforation of the bowel, obstruction due to knotting of the tube, and postcricoid ulceration due to prolonged use of the tube.

In acute obstruction or chronic obstruction with marked distention, cecostomy has been performed for decompressive purposes. When complete diversion of the fecal stream is desired, transverse or sigmoid colostomy with division of the bowel is carried out. This is followed by repeated irrigations of the distal segment of bowel. Such therapy carried out over a period of 2 to 4 weeks permits restitution to normal of the previously obstructed, edematous, distended, and highly infected segment of colon.

We have made practically routine use of preoperative, operative, and postoperative transfusions. Anemia is not the sole indication for transfusion. Dehydration is combatted by parenteral as well as oral administration of appropriate fluids. Special care is given the urinary tract during the preoperative period, specifically in patients with cancer of the rectum. All these patients are under the careful supervision of a specially trained competent clinician who is assigned to the surgical service for this purpose. There is the closest collaboration between the surgeons and this physician at all times. We emphasize this feature as an important and desirable part of the program of the care of these patients.

Mention should be made of the routine preoperative administration of sulfanilamide

in the preparation of these patients. The senior author in collaboration with Seley reported, in 1938, the results of observations in 28 patients so prepared. These observations were controlled by careful bacteriological studies, and the opinion was expressed at that time that the incidence of postoperative peritonitis and wound infection seemed to be greatly reduced by the preoperative use of sulfanilamide. Since then, the drug has been given routinely to all patients with cancer of the large bowel. With this larger experience, we are more than ever convinced that this drug has real value in the prevention of infection. Meleney, in a recent communication, has submitted convincing evidence that the oral or parenteral administration of sulfonamides is many times more effective than its local application. However, it must not be forgotten that great importance is also attached to other details of preoperative preparation such as bowel decompression, transfusion, general rehabilitation, etc. While on the subject of sulfonamide therapy, it might be desirable to point out that the recent extensive use of the sulfonamide drugs, especially locally in the abdomen, has created among surgeons a false sense of security. While we do not wish to minimize the beneficial effects of these drugs when judiciously and carefully applied, we must emphasize that they should not be permitted to supplant careful preoperative and postoperative care and sound surgical technique. After all, the basic principles of surgery are of prime importance and must be followed, sulfanilamide or no sulfanilamide. It has been our impression that there is a tendency for many surgeons to relax their previously rigid technique because of an unwitting subconscious assurance that sulfanilamide would take care of everything. The use of sulfonamides in general surgery is practically in its infancy, and it is important that we employ these drugs with critical care so as to appraise their efficacy thoroughly. Unbounded enthusiasm is not warranted in the light of experience to date.

There has been no routine anesthesia in this group of patients. In the majority of cases, cyclopropane or ethylene with or without ether has been used. Some of the members of the service have used spinal anesthesia. More recently, we have employed the continuous spinal anesthesia after the method of Lemmon. The choice of the anesthetic agent has, in the majority of cases, been delegated to the anesthetist. An effort has been made to individualize each patient and to pick the anesthetic agent for the particular problem at hand. In the same way, we have chosen a particular operative procedure to take care of the individual problem presented by each patient. Individualization of the patient has been the prime consideration at all times.

POSTOPERATIVE COMPLICATIONS

The pulmonary complications have not been severe, and have influenced the mortality figures in only 3 instances. A severely toxic influenzal bronchopneumonia caused the death of a patient who had had an abdominoperineal resection. The postmortem findings were typical. The second patient also had an abdominoperineal resection and died of bronchopneumonia, which was verified at autopsy. In the third instance, a one stage ileocolic resection, the proven cause of death was bronchopneumonia. The great majority of postoperative pulmonary infections have responded quickly to sulfonamide therapy. It is apparent that these drugs have changed completely the prognosis of postoperative pulmonary complications.

The cardiovascular complications have worried us a great deal. In the entire group reported in this paper, the cause of death was proved by autopsy to be due to cardiovascular accidents in 6 instances: 5 were due to coronary thrombosis and 1 to cerebral hemorrhage. As stated before, we are particularly wary of the patient who has had a recent coronary occlusion and it would seem that the best policy is to defer surgery until cardiac reserve has been considerably improved. These patients represent a special problem which requires complete rapport between physician and surgeon. While the risk of radical surgery is greatly increased in this group, we do not believe that they should be denied the opportunity of cure of a malignant disease. We have carried out successfully extensive surgical procedures in a number of patients with severe

cardiac disease. Here the principle of individualization is particularly applicable.

The problem of wound infection after surgery of the colon has always been an important one. In the 192 operative procedures carried out in the present series, there were 22 wound infections, an incidence of 11.4 per cent. In no instance was the infection severe enough to contribute to the patient's death. We have made every effort to curtail wound infection by the following measures: (1) preoperative administration of sulfanilamide, (2) careful protection of the abdominal wall during the course of the operation, (3) rigid technique during suture anastomosis, (4) drainage through counter incisions, (5) ablating the mobilized segment of bowel when carrying out obstructive resections only after the abdominal wall has been completely repaired, and (6) the use of sulfanilamide locally in the abdominal wound. We have not been enthusiastic about the last, because infections have occurred in spite of it and because it is our clinical impression that the local use of the drug delays wound repair. We believe that, after the removal of large infected tumors, as found in the cecum and hepatic flexure, the skin and subcutaneous tissues should be packed and left open. It must be remembered in these cases that the entire bowel wall is permeated with organisms, and in spite of rigid technique the abdominal wound becomes contaminated. It is too much to expect primary wound healing under such circumstances. For the same reason, we always institute liberal drainage of the retrocolic tissues. Perhaps this is the important reason why we have not encountered to date a retrocolic infection severe enough to impair the recovery of the patient.

The problem of wound dehiscence and evisceration has always given the surgeon considerable cause for worry. It is well known that it is particularly prone to occur in patients operated upon for abdominal cancer. About 2½ years ago, after 4 instances of wound evisceration occurring in rapid succession, we changed our technique of abdominal wall suture. Since then we have used, routinely, fine alloy steel wire in the form of buried figure-of-eight sutures after the method originally described by T. E. Jones of Cleveland. During the succeeding 2½ years, in a large series of ward and private patients (over 1000), there has not been one instance of wound disruption. We have found this method of wound repair particularly applicable in the following situations: (1) after gastric resection for ulcer or carcinoma, (2) after cholecystectomy in muscular individuals, (3) after operation for colonic cancer, ulcerative colitis and regional ileitis, (4) after splenectomy, and (5) following hysterectomy through a subumbilical median incision. In 3 or 4 instances, patients have complained of pain at the site of one of the sutures. This has been noted almost exclusively in upper right rectus incisions. In each case, the pain gradually disappeared and it was not necessary to remove the offending suture. When infection of the wound occurred, the wire sutures held the tissues together, there seemed to be less fascial slough than usual, and frequently the sutures were covered by granulation tissue without delaying wound repair or forming sinuses. Usually, however, in the presence of infection, the sutures loosened and were removed as the infection subsided. We have been very much impressed with this method of wound closure and have no hesitancy in urging its more general use.

Bladder complications following resection of tumors of the rectum and rectosigmoid have been surprisingly infrequent. In 2 cases, the loss of vesical tone persisted for a considerable period, necessitating prolonged catheterization.

At the beginning of this study we employed the method of bladder drainage devised by Duke, of St. Mark's Hospital, London. This consists of a two way irrigation system through an indwelling catheter. Experience proved, however, that it was better to remove the catheter 24 hours after operation and encourage the patient to void spontaneously. In most instances, the patients began to void spontaneously on the 3d or 4th day. The few bladder infections that did occur were mild and responded quickly to irrigations and sulfonamide therapy. In 1 case the membranous urethra was accidentally injured during the perineal part of the operation. With an indwelling catheter in place, the opening

closed spontaneously without stricture formation.

There is one complication, fortunately occurring only once in the present series, which should be discussed. In going over the literature on the subject of colonic cancer, we were struck by the fact that this complication has been rarely talked about. We refer to the postoperative retraction within the abdomen of an exteriorized loop of bowel, as in the performance of an abdominoperineal resection or an obstructive resection. Experience has proved that this is a lethal complication in most instances. The surgeon must always consider the possibility of this complication and guard against it. While many theoretical reasons have been advanced for this unfortunate accident, we feel that, from the practical standpoint, it can be prevented by avoidance of any tension on the exteriorized segment of bowel. The bowel should project 2 or 3 inches beyond the skin surface. This requires the operative mobilization of sufficient colon to permit exteriorization in the relaxed position. Experience has also proved that a distended colon, filled with feces, the result of chronic intestinal obstruction, should rarely, if ever, be subjected to resection.

ANALYSIS OF CASES FOR PERIOD JULY 1, 1937, TO JULY 1, 1941

Carcinoma of the cecum, ascending colon, and hepatic flexure. With unobstructed neoplasms of the right colon, we have favored a two stage operation. At the first stage, through a left rectus incision, operability is determined and a side-to-side ileotransverse colostomy or an ileosigmoidostomy is performed after division of the ileum close to the cecum. The second stage, carried out 3 or 4 weeks later through a right rectus incision, consists of an ileocolic resection to include the hepatic flexure, with drainage of the retrocolic tissues. If the first stage is performed through a left sided incision, the second stage will be much easier because of the absence of adhesions on the right side of the abdomen. We wish to emphasize this feature. Our experience with the obstructive resection operation proposed by Lahey for right sided tumors has been unsatisfactory and we have abandoned it.

TABLE I.—CANCER OF RIGHT COLON

Operations	Cases	Deaths	Per cent Mortality
Two stage resection completed	7	0	0
One stage resection	6	2	33.3
Ileocolostomy, ileostomy, Lahey operation, etc.	17	8	47
Total	30	10	
Operable cases	13		
Operability per cent	43.3		

During the 4 year period referred to, we have had 30 cases of cancer of the right colon (Table I): 6 of the cecum, 16 of the ascending colon, and 8 of the hepatic flexure. Thirteen cases were found operable at the time of exploration, an operability percentage of 43.3. In the 17 remaining patients, inoperability was indicated by hepatic metastases in 12, hepatic and peritoneal metastases in 3, and peritoneal involvement in 2. In 6 instances, a one stage resection was carried out, 5 by the usual suture anastomosis and 1 by the obstructive resection of Lahey. There were 2 deaths. The cause of death in one, as verified by autopsy, was bronchopneumonia and a localized abscess in the right lumbar gutter. There was insufficient drainage in this case. The second patient, a 71 year old woman on whom the Lahey operation was performed, succumbed 2 days after the colostomy was closed, subsequent to a trying convalescence following the first operation. There was no postmortem examination.

In a group of 7 patients, in whom the two stage operation was completed, there was no operative mortality. In another group of 14 cases, an ileotransverse colostomy or an ileosigmoidostomy with exclusion of the terminal ileum was performed. In 10 instances, inoperability precluded further surgery. There were 5 deaths in this group of 14 patients. Two, both operable, died of cardiac failure, as demonstrated at autopsy. A third patient, also with an operable lesion, died of a mechanical ileus because the wrong end of ileum was anastomosed to the colon. We wish to emphasize the care that should be exerted in visualizing the correct segment of ileum before carrying out the anastomosis. The fourth death occurred in an operable neoplasm of the hepatic flexure and, at autopsy, the cause was

TABLE II.—CANCER OF TRANSVERSE COLON

Operations	Cases	Deaths	Per cent Mortality
Obstructive resection	5	1	20
Ileocolostomy, cecostomy	3	1	33.3
Total	8	2	
Operable	5		
Operability per cent	62.5		

found to be a generalized peritonitis. The suture line was intact. The fifth death occurred in an inoperable case and the postmortem examination disclosed generalized metastases. There was no indication of infection.

The 3 remaining cases of the total group of 30, died after operation. One, a neoplasm of the cecum involving the ileocecal region, was admitted with marked acute intestinal obstruction. Ileostomy was performed. At postmortem examination, the cause of death was found to be a generalized peritonitis due to free perforation of the tumor itself. The second patient succumbed after a Lahey operation for carcinoma of the ascending colon. Autopsy disclosed extensive lymph node metastases and a local peritonitis. We believe that this operation was a bad choice and that the surgeon should have been content with a short-circuiting procedure. The last patient was subjected to incision and drainage of an intra-abdominal abscess due to perforation of a cecal tumor. Autopsy revealed extensive liver and peritoneal metastases. There was no evidence of peritonitis.

Transverse colon. For operable tumors of the transverse colon, we prefer the operation of obstructive resection with excision of a wide section of mesocolon. We are convinced that, for the majority of surgeons, this procedure is the most radical and the safest. We do not believe that an end-to-end suture anastomosis of the transverse or left colon should be carried out unless there has been a previous complete diversion of the fecal current proximal to the site of suture. Diversion of the fecal stream cannot be obtained unless the bowel is transected, as, for instance, in the Devine operation. The surgeon who routinely attempts to carry out primary resections and anastomoses will find that he is unconsciously skimping on the amount of bowel excised on each side of the neoplasm in order to prevent tension on the suture line, and will, therefore, note a higher percentage of recurrences. We have not been impressed with the need for the Devine operation for cancers of the left colon because this procedure entails 2 major stages and 1 of a minor nature. The same can be accomplished by the 1 major stage and the minor extraperitoneal colostomy closure of the obstructive resection operation. We believe the Devine operation is particularly applicable for small tumors at, or just above, the rectosigmoid where an obstructive resection could not be carried out because of technical difficulties and where an abdominoperineal resection would, perhaps, constitute an unjustifiably radical procedure.

The results of attempts at sterilization of the contents of the large bowel in the human by the use of sulfaguanidine or succinylsulfathiazole have not been conclusive enough to warrant any undue enthusiasm or to employ operative procedures, such as primary suture anastomoses, which the surgeon would ordinarily never undertake. Perhaps the future will bring such revolutionary changes in chemotherapy that we will be able to revise completely our present methods of handling cancers of the left colon.

Of 8 cases of carcinoma of the transverse colon (Table II), 5 were found to be operable; i.e., 62.5 per cent. There was 1 death in this group of 5 obstructive resections. This patient died on the 5th day, apparently of a cerebral hemorrhage. There was no autopsy. In the 3 remaining cases, ileosigmoidostomy with exclusion was carried out in 2, and cecostomy in 1. One of the patients having an ileosigmoidostomy died and the postmortem examination revealed hepatic metastases and extensive bronchopneumonia. The peritoneal cavity was clean.

Splenic flexure, descending colon, and sigmoid. There are 40 patients in this group (Table III), 25 males and 15 females. Twenty-eight were found operable, an operability percentage of 70. In 27 instances, obstructive resection was carried out with 1 fatality. This patient, with a descending colon tumor, died on the 5th day with the clinical and cardiographic signs of an acute coronary closure.

TABLE III.—CANCER OF LEFT COLON AND SIGMOID

Operations	Cases	Deaths	Per cent Mortality
Obstructive resection	28	1	3.5
Colostomy	8	6	75
Ileosigmoidostomy	2	0	0
Exploratory laparotomy	2	0	0
Total	40	7	
Operable	28		
Operability per cent	70		

There was no postmortem examination. The 28th case consisted of a sigmoidostomy for a malignant adenomatous polyp. The operative mortality in this group was 3.5 per cent.

In the 12 remaining cases, colostomy was performed in 8, ileosigmoidostomy in 2 and exploratory laparotomy in 2. There were 6 deaths, the essential details of which are as follows:

1. Cecostomy for intestinal obstruction was performed due to tumor of sigmoid. Convalescence was complicated by embolization of femoral artery. Death was probably due to myocardial infarction. No autopsy was performed.
2. Cecostomy was performed for perforated inoperable tumor of sigmoid. Passage of Miller-Abbott tube was unsuccessful. Death due to obvious peritonitis followed. No autopsy was done.
3. Colostomy was performed for inoperable perforated cancer of sigmoid. Autopsy revealed generalized metastases and a pelvic peritonitis.
4. This patient was a woman of 77. She had an obstructing carcinoma of the splenic flexure. Cecostomy was followed by ileosigmoidostomy. Death was due to cardiac failure. Postmortem examination revealed liver metastases.
5. Colostomy was performed for perforated tumor of sigmoid. Diffuse peritonitis was found at autopsy.
6. Colostomy for carcinoma of sigmoid with perisigmoidal abscess and perforation of bladder was done. Postoperative disruption of the wound followed. Death was due to peritonitis from spontaneous perforation of jejunum and transverse colon.

It will be noted that spontaneous perforation of a colonic neoplasm constitutes a particularly lethal complication and that, in spite of intensive sulfonamide therapy, locally and parenterally, the mortality is very high.

Rectosigmoid and rectum. It is not our purpose to discuss at length the various arguments for or against the many operations recommended for cancer of the rectum. Suffice it to say that, for the majority of the patients that we see, we favor the one stage abdominoperineal resection of Miles with a permanent colostomy placed in the midline below the umbilicus. For elderly patients with low lying tumors, we employ the Lockhart-Mummery procedure of preliminary colostomy and posterior resection. If a two stage operation is indicated because of chronic obstruction, a cecostomy is performed as the first step and an abdominoperineal resection as the second. For small tumors located at, or just above, the rectosigmoid, we favor the Devine colostomy followed by anterior resection with end-to-end anastomosis. We rarely perform the two stage Lahey operation for the following reasons: The second stage has, in our hands, been a more difficult operation than the one stage abdominoperineal resection; and with preoperative sulfonamide therapy, the operation becomes unnecessary as a routine measure. If chronic obstruction is present, we believe that cecostomy is safer than the first stage of the Lahey operation.

TABLE IV.—CANCER OF RECTUM AND RECTOSIGMOID

Operations	Cases	Deaths	Per cent Mortality
One stage combined abdominoperineal resection	36	6	16.6
Two stage Lahey operation	7	0	0
Two stage Jones operation	3	1	33.3
Hartman operation	2	1	50
Lockhart-Mummery operation	1	0	0
Colostomy	2	1	50
Inoperable cases	34	11	32.3
Total	85	20	
Operable cases	51		
Operability per cent	60		

In this group there were 85 patients who were subjected to operation (Table IV). Fifty-one were found operable, an operability of 60 per cent. In 36 cases, a one stage abdominoperineal resection was carried out with 6 deaths, or an operative mortality of 16.6 per cent. The causes of death were as follows:

1. The patient developed extensive bronchopneumonia. The peritoneal cavity was clean. This was verified by autopsy.
2. The patient had a coronary occlusion with myocardial infarction. This was verified by autopsy.
3. Mechanical ileus was unrelieved by enterostomy. The clinical course was not that of peritonitis. No postmortem examination was performed.

4. There was wound disruption with death occurring after resuture. This case was seen before routine use of wire sutures. No preoperative sulfanilamide was given. Death was probably due to peritonitis; no autopsy was done.

5. Fulminating influenzal bronchopneumonia developed; this was verified by autopsy.

6. The patient had peritonitis with paralytic ileus. No postmortem examination was performed. No preoperative sulfanilamide was given.

In the 15 remaining cases of the operable group the following operations were carried out: 7 two stage Lahey operations, 3 two stage Jones operations, 2 Hartman procedures, 1 Lockhart-Mummery procedure, and 2 preliminary sigmoid colostomies. There were 3 deaths in this group:

1. The Hartman operation had been done. Autopsy disclosed that death was due to a spontaneous perforation of the colostomy loop with peritonitis. A pulmonary embolus was also found.

2. A sigmoid colostomy had been performed. Chronic obstruction was present on admission to the hospital. Death was caused by paralytic ileus; this was confirmed by autopsy.

3. A sigmoid colostomy had been done. Patient died of peritonitis consequent upon a spontaneous perforation of a rectosigmoid neoplasm subsequent to the performance of the colostomy.

The total mortality for the operable group was 17.6 per cent.

Thirty-four patients were pronounced inoperable for the following reasons: hepatic metastases, 11 cases; inseparable neoplastic fixation to adjacent structures such as bladder, small intestine, etc., 9 cases; extreme old age or poor physical condition, 7 cases; extensive peritoneal metastases, 2 cases; metastases to tibia as proved by biopsy, 1 case; free perforation with peritonitis, 4 cases. There were 11 operative deaths. The details, given briefly, are as follows:

1. The first stage of a Lahey operation for inoperable tumor was done. Autopsy revealed extensive metastases.

2. Cecostomy for perforated inoperable tumor of rectosigmoid was performed. Generalized peritonitis was disclosed at autopsy.

3. Cecostomy for perforated cancer of rectosigmoid was carried out. Patient was practically moribund at time of operation. The cause of death was peritonitis.

4. Colostomy was done for perforated tumor of rectosigmoid. The cause of death was peritonitis.

5. Colostomy was performed for inoperable tumor with hepatic metastases. The postmortem examination disclosed pulmonary embolus.

6. Colostomy for inoperable growth of rectosigmoid with obstruction was performed. The autopsy revealed a perforated tension ulcer of the cecum with peritonitis.

7. Patient had perforated growth of rectosigmoid. The operation consisted of drainage of pelvic abscess, and death was probably due to peritonitis. No autopsy was performed.

8. Colostomy was carried out for cancer of the rectum with frozen pelvis. The autopsy disclosed a pulmonary embolus and a small liver abscess.

9. Colostomy for inoperable tumor of rectum was done. Death was caused by pneumonia and cardiac failure, as disclosed by autopsy.

10. Colostomy for inoperable tumor of the rectum was performed. No autopsy was done.

11. First stage of a two stage Jones procedure was carried out. Autopsy disclosed a perforation of the inverted distal loop with peritonitis, probably caused by interference of blood supply at the time of operation. The tumor was inoperable.

SUMMARY AND CONCLUSIONS

1. Many of the patients admitted to the wards of the Mt. Sinai Hospital present complicating medical conditions which influence, to a large extent, morbidity and mortality of major surgical procedures.

2. It is important, therefore, to extend the preoperative period of rehabilitation in patients with colonic cancer so as to minimize the effects of these complicating illnesses.

3. In the series of cases reported in this paper, operability has been influenced more by conditions associated with the growth itself than by such general considerations as age of the patient, obesity, anemia, etc.

4. Free perforation of a carcinoma of the colon is a lethal complication in most instances.

5. The use of the Miller-Abbott tube in the preoperative and postoperative period is particularly emphasized.

6. It has been our experience that the preoperative oral administration of sulfanilamide has been a greater factor in decreasing the incidence of postoperative wound infections and peritonitis than the use of the drug locally at the time of operation.

7. Undue enthusiasm concerning the local application of sulfonamide drugs in colonic surgery is not warranted in view of experience to date.

8. Postoperative pulmonary complications have been most beneficially influenced by the sulfonamide drugs.

9. The cardiovascular complications constitute the major cause of postoperative morbidity and mortality in this series.

10. It is our impression that wound infection has been curtailed to a great extent by the preoperative administration of sulfanilamide.

11. We have, so far, eliminated the complication of wound disruption by the use of buried alloy steel wire.

12. Attention is called to a rarely mentioned postoperative complication following colonic surgery; namely, retraction within the abdomen of a loop of bowel.

13. For carcinomas of the right colon we favor the two stage ileocolic resection, with a 3 week or 4 week interval between the operative procedures. There was no operative mortality in this group.

14. We favor the operation of obstructive resection with excision of a wide section of mesentery for neoplasm of the transverse and left colon. The mortality in this group was 3.5 per cent.

15. We believe that a suture anastomosis of the left colon should not be carried out unless there has been a preceding complete diversion of the fecal current.

16. For small carcinomas of the rectosigmoid we favor the Devine operation consisting of a transection of the transverse colon and a resection of the tumor-bearing portion of bowel with suture anastomosis.

17. For carcinoma of the rectum, our preference in most instances is the one stage Miles abdominoperineal resection.

18. For low-lying neoplasms in elderly individuals we believe the Lockhart-Mummery procedure has real value.

19. Finally, we wish to call attention to the fact that between 20 and 25 per cent of the patients admitted to the hospital with carcinomas of the rectum had undergone treatment for hemorrhoids during the preceding 2 to 5 months. This emphasizes the importance of a carefully performed digital rectal examination followed by proctoscopic visualization in all patients who come to the physician, complaining of bleeding from the rectum.

UTERINE CONTRACTILITY DURING LABOR AND THE EFFECTS OF PARITY AND DYSTOCIA UPON IT

A Study of 105 Patients with the Lóránd Tocograph

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THE present report deals with the uterine contractions of labor, as revealed by the Lóránd tocograph (1). It is based upon observations on a series of patients who were studied at repeated intervals throughout the greater part of their periods of labor. It concerns only certain aspects of the collected data; others will be reported upon at a later date. The following relationships are considered in this communication: (1) the influence of advancing labor, (2) the effect of parity, and (3) the effect of dystocia upon the contractions. As far as can be ascertained, no similar set of observations has been published.

MATERIALS AND METHODS

Ward patients admitted consecutively to the maternity floor of the Hospital of the University of Pennsylvania between March 22 and April 15, 1942, acted as subjects. These women received routine care which included the administration of morphine for analgesia and nitrous oxide oxygen ether for delivery.

Three trained nurses, each on 8 hour duty, secured the tocographic records of the contractions. The tocograph is a simply constructed mechanical recorder which detects uterine activity through the medium of the abdominal wall. It has been described in a previous report (2). The first tracing was made shortly after each patient was admitted; subsequent ones were secured at 1½ to 2 hour intervals. In most instances, the final tracing was made during delivery. Any unusual activity on the part of the patient, or any treatment that she may have received during the recording, which might have influenced uterine activity, was noted. A fourth year medical student recorded the clinical course of the patient's labor.

The tonus and the intermittent contractions of the uterus were studied. Each recording of uterine activity was evaluated in terms of 5 characteristics: (1) tonus, (2) wave height, (3) the sum of tonus plus wave height, (4) wave duration, and (5) wave frequency. In measuring the height, duration, and frequency of the contraction waves, the values resulted from taking the mean of 5 consecutive waves of each tracing.

The measurements are expressed in the accompanying tables in the following terms: tonus (4th column from the left) and wave height (i.e., strength of contractions, 4th column from the right) are recorded in millimeters which represent the distance traversed by the writing point of the tocograph; the duration of the contractions (2d column from the right) is expressed in seconds; and their frequency (right column) is the number occurring per hour.

The sum of the uterine tonus and wave height is listed in each table, 3d column. It is assumed that this combined value represents roughly the maximum effort of the uterus.

Where differences between values in the tables are stated as being significant, they were found to be more than 3 times greater than their standard errors. Significantly high values in Tables IV to VII inclusive are designated by *italics*.

RESULTS

General characteristics of patients. The study was limited to the first consecutive 105 patients admitted in labor who delivered vaginally. Thirty-four were primiparas and 71 were multiparas. Forty-nine were white and 56 were colored. Eleven individuals exhibited some degree of dystocia. The patients sup-

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TABLE I.—INFLUENCE OF ADVANCING LABOR UPON CONTRACTIONS OF 105 PATIENTS

Hours before delivery	No. patients	No. tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
			Mm.	Mm.	Mm.	Sec.	No. per hr.
18–23.9	17	38	3.0±2.8	4.8±2.8	7.1±3.7	158±88	12.1±4.0
12–17.9	22	52	3.3±1.0	4.8±2.7	7.9±3.9	132±58	14.8±9.5
6–11.9	44	98	3.5±3.5	5.6±3.1	8.6±4.7	135±62	17.1±7.8
0– 5.9	102*	264	4.5±4.0	5.9±3.2	10.0±4.5	115±51	22.1±8.4

*Records of 3 persons unsuitable for measurement.

Table I. Measurements made with a Lóránd tocograph of the uterine contractions of 105 patients, throughout the 24 hours preceding delivery. Tonus and height of contraction waves are expressed in the number of millimeters traversed by writing point of tocograph.

TABLE II.—INFLUENCE OF ADVANCING LABOR UPON CONTRACTIONS OF 34 PRIMIPARAS

Hours before delivery	No. patients	No. tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
			Mm.	Mm.	Mm.	Sec.	No. per hr.
18–23.9	11	27	3.2±3.0	4.9±5.2	7.4±3.3	154±65	11.6±3.3
12–17.9	14	31	3.5±3.3	4.3±2.3	7.6±3.7	136±59	14.5±7.6
6–11.9	23	55	4.5±3.9	4.4±2.3	8.7±4.6	135±62	18.0±8.3
0– 5.9	32*	92	5.5±4.3	5.1±2.5	10.1±4.6	109±43	23.6±7.7

*Records of 2 persons unsuitable for measurement.

TABLE III.—INFLUENCE OF ADVANCING LABOR UPON CONTRACTIONS OF 71 MULTIPARAS

Hours before delivery	No. patients	No. tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
			Mm.	Mm.	Mm.	Sec.	No. per hr.
18–23.9	6	11	2.4±2.4	4.6±3.8	6.2±4.4	171±128	13.3±5.1
12–17.9	8	21	2.8±2.2	5.3±2.3	8.2±4.4	126± 58	15.1±7.9
6–11.9	22	43	2.2±2.5	7.1±3.8	8.5±4.9	136± 60	15.9±5.1
0– 5.9	69*	172	3.9±3.8	6.3±3.6	9.8±4.1	118± 55	21.3±8.6

*Records of 2 persons unsuitable for measurement.

plied 452 tocographic records made within 24 hours of delivery. Few patients supplied tracings prior to that time; such records were omitted from consideration in order to simplify the presentation. The number of tracings per patient in the 24 hour period varied from 1 to 12 with an average of 4.3.

Influence of advancing labor upon contractions. Table I gives the mean values of the contractions of the 105 patients arranged according to the time in labor at which their records were secured. Note: (1) wide standard deviations of all measurements; (2) progressive *increase* in uterine tonus and the height and frequency of the contraction waves; and (3) progressive *decrease* in duration of contraction waves. The tonus of the uterus, the strength (wave height) and frequency of the contractions *increased* progressively as labor advanced; the duration of the contractions *decreased.*

Influence of parity upon contractions. The contractions of the primiparas can be compared with those of the multiparas in Tables II, III, and IV. Tables II and III show the influence of the progress of labor upon the con-

TABLE IV.—INFLUENCE OF PARITY UPON CONTRACTIONS THROUGHOUT THE LAST 24 HOURS OF LABOR

Parity	No. patients	No. tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
			Mm.	Mm.	Mm.	Sec.	No. per hr.
Primiparas	34	205	4.6±3.4	4.9±2.2	9.0±3.4	126±48	19.3±6.7
Multiparas	71	247	3.7±2.8	6.5±3.3	9.3±5.0	125±53	19.4±7.5

TABLE V.—INFLUENCE OF DYSTOCIA UPON CONTRACTIONS THROUGHOUT THE LAST 24 HOURS OF LABOR

Dystocia	No. patients	No. tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
			Mm.	Mm.	Mm.	Sec.	No. per hr.
None	94	379	3.8±2.9	5.5±2.8	8.6±4.1	116±46	20.0±7.4
Present	11	73	6.1±3.6	6.0±2.5	11.8±4.4	166±83	17.9±7.1

TABLE VI.—INFLUENCE OF DYSTOCIA UPON CONTRACTIONS OF 34 PRIMIPARAS

Dystocia	No. patients	No. tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
			Mm.	Mm.	Mm.	Sec.	No. per hr.
None	29	164	3.8±3.1	5.0±2.3	8.2±3.3	115±42	20.1±6.9
Present	5	41	8.0±4.5	4.4±1.9	12.5±4.3	163±73	17.5±9.0

TABLE VII.—INFLUENCE OF DYSTOCIA UPON CONTRACTIONS OF 71 MULTIPARAS

Dystocia	No. patients	No. tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
			Mm.	Mm.	Mm.	Sec.	No. per hr.
None	65	215	3.8±2.9	6.0±3.3	9.0±4.7	117±49	19.9±7.8
Present	6	32	3.7±2.5	8.1±3.3	10.9±4.5	169±96	18.4±2.4

tractions in the 2 groups. Table IV contrasts the measurements of both groups for labor as a whole. The primiparas experienced a significantly higher tonus than did the multiparas; the latter, on the other hand, exhibited significantly stronger contractions than did the former.

Influence of dystocia upon contractions. Eleven patients experienced unusual periods of labor from the mechanical point of view: (1) 7 infants engaged occiput posteriorly, of which number 2 failed to rotate to the anterior position, (2) 1 patient had an unusually large infant, (3) 2 experienced relative degrees of pelvic contraction, and (4) 1 woman had difficulty with a breech labor.

The influence of dystocia upon the contractions is recorded in Tables V, VI, and VII.

Table V records the effect of dystocia upon the contractions of the 105 patients as a single group, for their last 24 hours of labor. The dystocia significantly increased the tonus, the wave height plus tonus, and the duration of the contractions, but not the strength (height) of the contractions.

Table VI shows the influence of dystocia upon the contractions of primiparas. The dystocia significantly increased the tonus, the

wave height plus tonus, and the duration of the contractions.

Table VII records the influence of dystocia upon the contractions of the multiparas. In this group dystocia significantly increased the wave height (strength of contractions) but had no effect upon tonus. As in the case of the primiparas, it increased the duration of contractions. It had no significant effect upon the tonus plus wave height of multiparas.

EVALUATION OF STUDY

This study places on a statistical basis, for the first time, the generally accepted clinical observation of the progressive change in uterine activity which accompanies the advance of labor (Table I). It shows that change in activity can be detected early in labor, with the tocograph. It reveals one fact, perhaps not hitherto suspected, that the progress of labor *decreases* rather than increases the duration of the contractions (Table I), whereas the other characteristics increase in magnitude.

The investigation shows (Table IV) that primiparas experience a higher degree of tonus during labor than multiparas, whereas the latter exhibit contractions of greater magnitude. On the other hand, the patient's total effort, as measured by the sum of tonus and wave height, seems to be about equal both in primiparas and multiparas. The same is true of the duration and the frequency of the contractions.

Personal unpublished observations with the tocograph show that patients having rapid deliveries experience low tonus and high contraction waves. The high tonus of the primiparas, with their compensatory lower contraction waves, may be one of the chief factors responsible for the longer periods of labor in primiparas as a group. This observation would suggest the advisability of utilizing in the delivery of primiparas those methods which are directed especially at the lowering of tonus.

The present observations indicate that dystocia increases the effort on the part of the uterus. It augments the already high tonus of the primiparas, and also the already strong contractions of the multiparas; it does not increase the tonus of the multiparas or the wave height of the primiparas. Dystocia prolongs the duration of the contractions of all patients.

SUMMARY AND CONCLUSIONS

1. The advance of labor brings about a progressive *increase* in uterine tonus, strength of the intermittent contractions, total amount of energy expended, and frequency of contractions. It shortens the duration of the contractions.

2. Primiparas experience a significantly higher tonus throughout labor than do multiparas.

3. Multiparas experience significantly stronger contractions throughout labor than do primiparas.

4. Dystocia significantly increases the already high tonus of primiparas and the already strong contractions of the multiparas. It prolongs the duration of the contractions of all patients.

5. The Lóránd tocograph offers a suitable means for studying the contractions of the human uterus throughout labor.

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A STUDY OF THE POSTERIOR URETHRA IN THE NEWBORN FEMALE

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DURING the past 11 years there has been more research on the female urethra than at any other time. The many unexplained symptoms referable to the female lower urinary tract has prompted this research. Twinem states that the female urethra has become only the resting place for the cystoscope in investigating the bladder. Many prominent urologists have undertaken the study of the female urethra with the idea in mind that the understanding for such symptoms would be found here.

The first investigators concluded that there were glands throughout the entire urethra, and that the group of glands found in the posterior urethra were the cause of many of these symptoms.

The purpose of this paper is to determine (a) the presence or absence of glands in the posterior urethra, (b) the nature of the folds of the urethra, (c) the structure of the urethral wall, and (d) to list and interpret other histological findings.

HISTORY

These glands were said to be the homologue of the prostate in the male and reacted to infection in much the same manner as the prostate. For several years this remained the accepted basis for lower urinary tract symptoms in the female. Two investigators studied serial postmortem sections of the urethra in all decades of life. They found Skene's glands in the anterior third and some glandular structures and parts of Skene's glands in the middle third. At no time, however, were glands found in the posterior third of the urethra. Some workers felt that those structures which were mistaken for glands were in reality folds of the mucous membrane. These findings were confirmed by later investigators. Before long two different schools of thought developed as to the structure of the posterior urethra. One group were of the opinion that there were glands homologous to the prostate in the posterior third and the other believed there were none.

Folsom, in writing on the subject of the female urethra in 1931, cited a series of chronic urological cases which were referred to him. In each case the symptoms were burning, frequency, and "cold in the bladder" over a long period of time. These cases had had a thorough examination with pyelograms and kidney function tests of the upper—kidney, urethra, bladder—tract; the bladder and trigone had been studied carefully with the cystoscope; yet, nothing could be found to account for the symptoms. The urethra was completely neglected in each instance. Folsom observed a marked inflammatory process in the posterior urethra of these females and described a "collarette" formation at the vesical neck in some. There was abundant growth of tissue in this region and it was "nicknamed" the "female prostate." Because of the chronicity of symptoms and persistence of tumefactions in the posterior urethra of these females, particularly at the vesical neck, he believed there must be glandular elements in these tissues which would be the site of enlargement or the basis of chronic inflammation. Several photomicrographs were shown demonstrating glandular elements in the posterior urethra.

Interest in this subject was stimulated and McKenzie and Beck, in 1936, cut 50 postmortem specimens of female urethrae longitudinally in an effort to determine whether or not there were glands in the urethra and the exact nature of the mucous membrane. Nineteen cases were in the first decade of life. Five of the specimens of children were cut serially. All others were cut every 100 micra. They concluded that there were 2 types of normal bladder neck and urethra: (a) smooth

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mucous membrane with no invagination, and (b) mucosal invagination (seen in 3 of 17 children). There were also some periurethral tubular structures in the anterior and middle thirds of the urethra in 3 of 17 children, but no glands were found in the posterior urethra.

At about the same time, Cabot and Shoemaker reported 59 routine postmortem cases, 19 of which were in the first decade of life. Here, too, sections were cut longitudinally, and the urethra was laid open by cutting through the roof. In 32 cases there were groups of epithelial cells in the submucosa. Two cases showed secretory (mucin) epithelium replacing transitional epithelium in some areas; but no true glands were found. No evidence of glands was found in infants from 6 months' gestation to term. Two points established at this time were (a) the behavior of gonorrhea in women bears out the fact that there are no glands in the posterior urethra, and (b) that females with lesions of the urethra show normal urine.

To go further back for the opinions of earlier men in relation to the female urethra, we find the first reference by Virchow in 1853. He saw concretions in "urethral glands" of old women and deduced that urethral glands of females were homologous with the prostate in the male. In 1889, Tourneux found glands along the entire female urethra and stated that they were similar in structure to prostate glands of the 5 month old male fetus. In 1893, von Brunn described buds and epithelial nests. Those submucosal epithelial structures connecting with the mucous membrane were called "buds" or sprouts and those having no connection with the mucous membrane were termed "nests." He believed that these were stimulated by inflammation of the mucous membrane. At no time did he find glandular elements or secretory changes in the cells.

In 1894, Lubarsch stated that the cysts found in cell nests of von Brunn were due to central necrosis. He described the cysts arising in the urethra as originating in one of 3 ways: (a) von Brunn's cell nests with central necrosis, (b) inflammatory closure of crypts of the mucous membrane, and (c) abnormally placed glands in the urethra. In the same year Aschoff could *not* find von Brunn's buds, nests, or cysts in urethras of children from 1½ to 3 years of age and concluded that they must be of inflammatory origin.

In 1906, Herxheimer found von Brunn's nests in 11 of 29 cases and agreed that they were of inflammatory origin but that the elimination of toxic substances in the urine is stimulus enough to cause them in the newborn. In 1907, Giani did some excellent experimental work in rabbits dealing with this problem. By placing gelatin capsules containing tubercle bacilli in the bladder he was able to produce cystic areas in the mucous membrane of 20 rabbits. In 1911, Evatt modelled the urethra of a 3½ month old human fetus and concluded that "all glands of the female urethra are homologous to the prostate in the male. This would indicate that the female urethra is the counterpart of the whole prostatic urethra in the male."

In 1922, Franklin P. Johnson worked out the development of the female urethra and modelled the urethrae in the 60 and 75 millimeter fetus. He concurred with Lowsley in that he was not able to find any prostatic glands in the 50 millimeter embryo but he clearly saw them in the 55 millimeter embryo. He also reported glands along the entire urethra in the 215 millimeter embryo. He then dissected free an adult female urethra and made transverse sections of it at different levels; (a) the section near the bladder neck showed flattened urethra and folds in the anteroposterior direction with "8 layers of epithelium and a few simple tubular glands or ducts were seen lying close to the urethral epithelium and penetrating the submucosa for only a short distance"; (b) a section of middle third showed irregular folds. The glands here were more numerous, larger, more branched, and penetrated the submucosa for a greater distance. The glands had thick epithelial walls and they were lined by 1 to 3 layers of cuboidal epithelium, and (c) a section of the lower third showed more folds and more glands and branches.

M. J. Renner, writing on the female prostate and concretion formation in the female urethra in 1931, examined the urethra and trigones of 2 postmortem specimens which

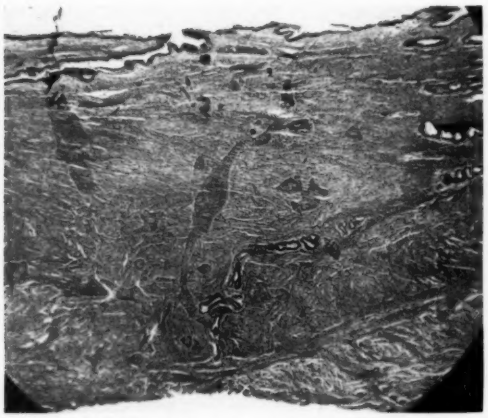

Fig. 1. Longitudinal section of anterior half of urethra. Bulk of Skene's glands at right. Deep penetration of glands in lower mid portion. Long glandular structure seen opening into urethral lumen upper mid portion. ×26.

Fig. 2. Longitudinal section from the posterior half of the same urethra as shown in Figure 1. No glandular structures are evident in this microscopic section. ×26.

were diagnosed as "concretion formations in the muscularis mucosae of a female urethra." In each case acinous and tubular glands were found in the posterior urethra. In one case they were also found in the trigone. Six other specimens of female urethrae were sectioned and, in each instance, glands were found in the posterior urethra. He believed that the concretions originated in rudimentary prostatic portions. No concretions were ever found in the Brunn nests. The fact that the concretions penetrated deeply seemed to point to their prostatic origin.

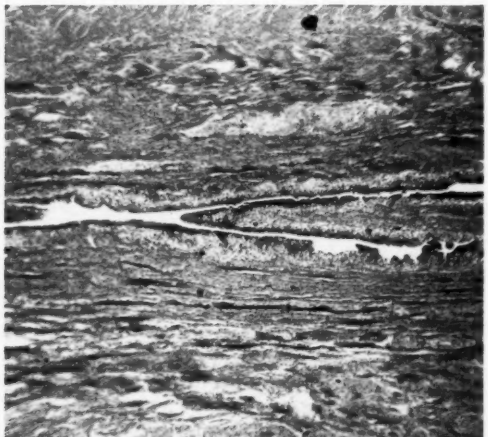

Fig. 3. Confusing fold seen in a longitudinally cut section. ×78.

Patch and Rhea, in 1935, believed that the cysts in Brunn's nests were the result of a secretory process in which tall columnar cells developed at the expense of surrounding cells and secreted mucin which was demonstrated by sections stained by mucicarmine. They believed that an irritated mucous membrane may undergo such metaplasia. These changes were followed microscopically by the authors in the exstrophic bladder of a 3 year old child.

Young, in 1940, reported a case of complete urinary retention in a female 66 years of age, cured by removing the obstruction with the cold cutting punch instrument. Sections of the tissue removed showed inflammation of periurethral glands and the production of marked local fibrosis. Thompson, on the other hand, reported 24 cases of vesical neck obstruction in the female which were relieved by resection. The resected specimens were studied microscopically, and in no instance were glands of any kind found and he could give no reason for the cause of the obstruction. However, he proposed, as a possible explanation, that hyperplasia of the epithelium or hypertrophy of the sphincter muscle occurs and causes retention.

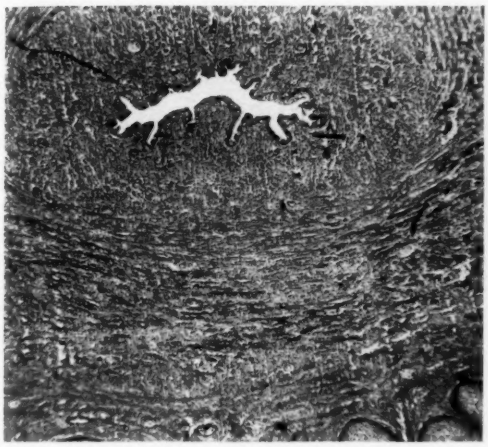

Fig. 4. Cross section of urethra with all its walls intact. ×31.

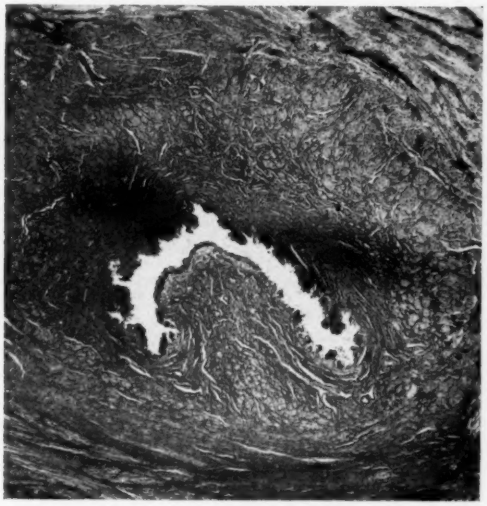

Fig. 5. Cross section illustrating prominent crista urethralis. This is the large fold of muscularis mucosae forming the floor. ×31.

Because of these conflicting findings by so many competent urologists, it was thought that a careful study of the normal urethra, particularly in its proximal one-third where all the pathological conditions under question exist, might help to throw some light on this problem. The urethra of the newborn infant would be the least apt to have been exposed to infection or trauma and, therefore, least apt to have its true anatomy and histology distorted. This may approach the microscopic picture of the normal female urethra. Reference will be made particularly as to the presence or absence of glands in the posterior urethra.

MATERIAL AND METHODS

Postmortem specimens were obtained from 21 fullterm infants ranging in age from 14 months to stillborn. Two additional specimens were obtained from 7 month premature infants who had lived for 24 hours. A third additional specimen was taken from a 7 month old premature infant who was stillborn. The specimens were removed from the body *in toto;* that is, the entire length of the urethra with the bladder intact and part of the vagina. This was done by splitting the symphysis pubis. The body of the bladder was then removed and all retained urine was expelled. The urethra was then measured from the neck of the bladder to the meatus and from the neck of the bladder to the interureteric ridge of the trigone. The trigone was then cut away from the neck of the bladder, labelled, and saved in a bottle containing 4 per cent formaldehyde. The anterior two-thirds of the urethra was then cut away from the posterior third, labelled, and placed in a separate bottle. A study was then made of the posterior urethra alone, and it is hoped to continue the investigations into the trigone or into the anterior urethra. All specimens were fixed in the usual manner in 4 per cent formaldehyde. Seven of the first specimens were sectioned longitudinally after the ure-

Fig. 6. Cross section showing cavernous tissue under higher magnification. ×64.

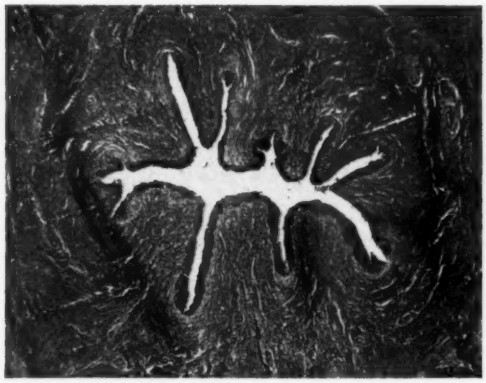

Fig. 7. Odd shaped urethra seen in cross section. Urethral wall divided into 9 separate folds. ×27.

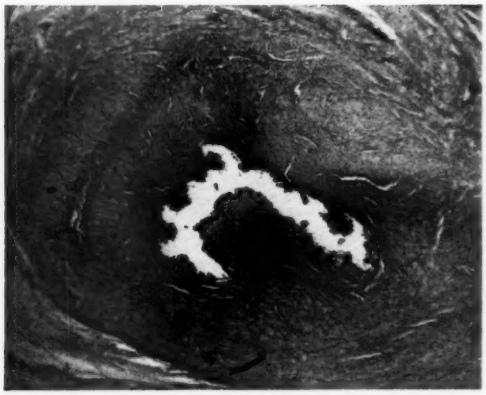

Fig. 8. Lymphocytic infiltration about the urethra. Heavily infiltrated tabs are seen hanging from the superior wall of urethra on the right. ×27.

thra had been laid open by cutting through the roof. The 3 following sections were cut transversely after the urethra had been laid open and 14 were cut transversely with all sides of the urethra intact. Notes were made on all macroscopic findings. The muscular layers of the urethra as well as the superior wall of the vagina were included in each specimen for orientation.

The specimens cut longitudinally were sectioned serially every 30 to 50 micra starting in the center of the floor and moving laterally. The posterior urethrae of all cross sections were cut serially every 5 to 8 micra. Hematoxylin and eosin was the standard stain used. However, it was soon discovered that by mounting all sections on slides and by staining only every fifth slide with hematoxylin and eosin it would be possible to use special stains on parallel interesting sections as they appeared. This method proved quite successful and the mucicarmine, the phosphotungstic-acid hematoxylin and the Mallory stains were used. Most pathologists agree that tissue structures are usually identified by the microscopic appearance and that special stains serve only as a helpful adjunct in certain cases.

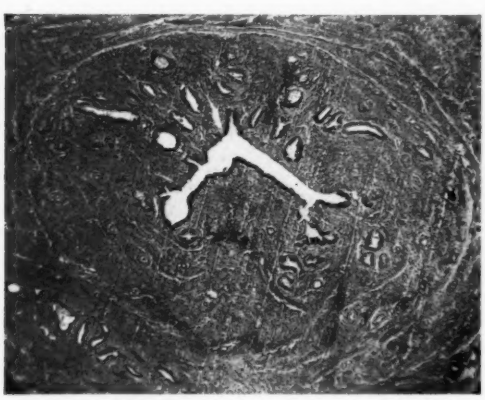

Fig. 9. Glandular structures surrounding the urethra seen at a glance. Group of glands seen lying on a bed of striated muscle in lower left-hand corner. ×27.

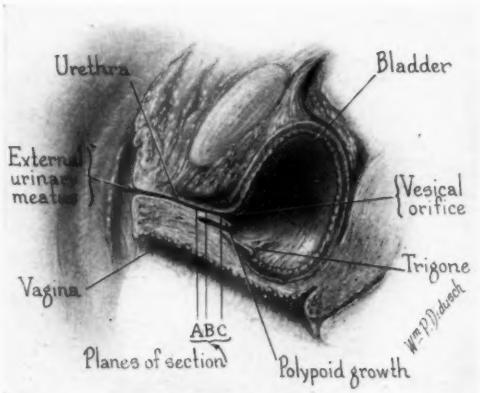

Fig. 10. Schematic drawing illustrating a polypoid growth in the posterior urethra. Planes of sections described at *A*, *B*, and *C*.

Fig. 11.

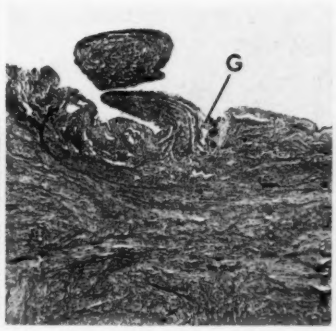

Fig. 12.

Fig. 13.

Fig. 11. Cross section of polypoid growth taken through its base. Intraepithelial gland seen at *G*. ×61.

Fig. 12. Section through *B*, in Figure 10, showing polypoid growth leaving the floor of the urethra. ×61.

Fig. 13. Cross section of polypoid growth nearer the bladder. Intraepithelial gland still present, *G*. ×61.

FINDINGS

In order to minimize possibilities of misinterpreting the description of findings, only the B.N.A. terms will be used. Instead of terms such as up, down, above, and so forth, the words cephalad, caudad, proximal, and the like will be substituted.

It is agreed by all that the paraurethral, compound tubuloalveolar glands of Skene are always found occupying the anterior third and sometimes the middle third of the urethra. Its ducts empty into the floor of the urethra just proximal to the meatus. These glands have been known to encircle the urethra completely. However, in no instance have Skene's glands ever been found extending into the posterior third of the urethra. With this in mind then, the groups of glandular structures in the posterior urethra cannot ordinarily be said to belong to Skene's glands. However, in this investigation, glandular structures found in the posterior third and found continuing distally were followed out into the middle third. The middle third was then sectioned serially to follow out the course of these structures. In other words, a distinct effort is made to study glands other than those of Skene. This study is limited as much as possible to the proximal third of the female urethra, i.e., the posterior urethra.

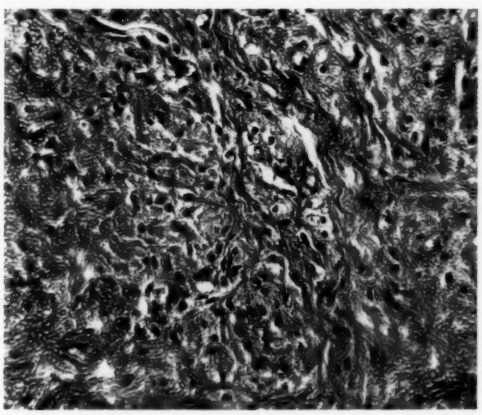

Fig. 14. High magnification of growth demonstrating its connective tissue character. ×310.

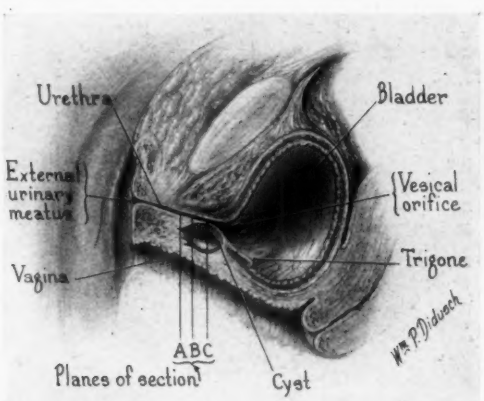

Fig. 15. Schematic drawing illustrating a huge cyst of the urethral wall in the posterior third.

Fig. 16. Section through distal end of cyst. This is seen as a small glandular structure in the lower left-hand corner. ×26.

A longitudinal section through the anterior half of a newborn urethra is shown in Figure 1. Considerable glandular tissue is seen in the upper right-hand side of the photomicrograph. It will be noted that Skene's glands penetrate practically the entire muscular coat of the urethra. These are seen in the central lower portion of the section. The terminal alveoli of these glands are made up of tall columnar epithelium. Duct structures close to the outlet of Skene's glands are lined by transitional epithelium. At the junction of the middle and anterior third a long glandular structure can be seen opening into the lumen with some mucus elements. This is demonstrated in this section and is seen emptying into the floor of the urethra at the upper center of the photomicrograph.

A longitudinal section of the posterior urethra of the same specimen is shown in Figure 2. Here we see transitional epithelium lining the urethra. The muscular coats are well described and there are no glandular structures.

It will be noted under "Material and Methods" that only the first 7 cases were cut longitudinally. A good reason for this is seen in Figure 3. A fold of the mucous membrane is seen in the lumen of the urethra in this section of the posterior urethra. This is quite confusing and such folds are entirely eliminated when cross sections are made. However, no glandular structures are seen in this photomicrograph.

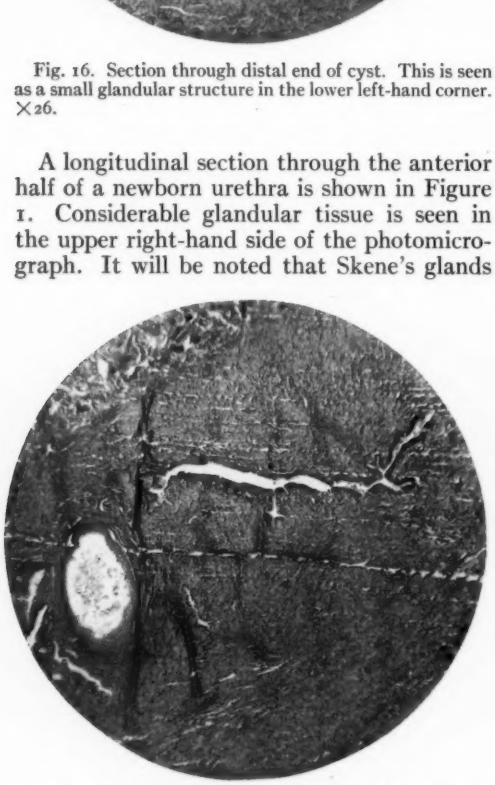

Fig. 17. Photomicrograph of a cross section of the cyst taken more proximally than that seen in Figure 16. Heavy layers of squamous cells have replaced glandular epithelium. ×26.

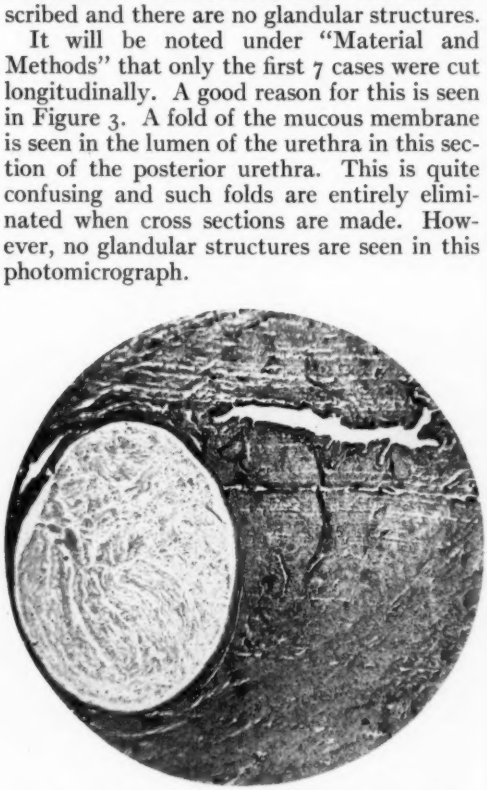

Fig. 18. Cross section of cyst taken at its broadest point. Its wall has been ruptured in the upper left-hand corner of the cyst where it is about to incorporate a neighboring gland. ×26.

When cross sections were made of the urethra with all its walls intact, a clear-cut well oriented picture was obtained. Such a picture is seen in Figure 4. This is the urethra of a 7 month old fetus. Folds of the urethra are clearly seen without the necessity of studying serial sections to eliminate them as glands. Small crypts are easily identified and the normal shape of the urethra is preserved. The crista urethralis is quite prominent and contains a good deal of cavernous tissue. Actually, the urethra is embedded in cavernous tissue. There are no glands seen in this specimen. The muscularis is well defined. The vaginal epithelium is clearly seen in the lowest portion of the figure and a very good picture of the thickness of the urethral floor is noted at a glance.

Another photomicrograph of a cross section of the posterior urethra of a newborn infant is seen in Figure 5. This illustrates very well the prominent crista urethralis and the cavernous tissue. Several small folds are seen projecting into the lumen of the urethra. The dark areas seen in this figure have no significance as they are merely an artifact concentration of stain. It is noted that no glandular structures exist in this posterior urethra. It may be well to add here that these are representative photomicrographs of the posterior urethra throughout. When it is stated that no glands are seen it is meant that no glands are seen in any other part of the posterior urethra.

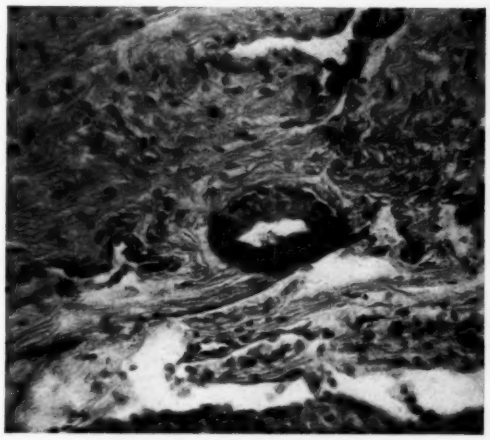

Fig. 19. Photomicrograph showing a glandular structure taking the mucicarmine stain. ×335.

A high power magnification of the urethral mucosa is shown in Figure 6. This effectively demonstrates the cavernous tissue and numerous blood sinuses. In this specimen no glandular structures were seen in posterior urethra.

Fig. 20. Cross section through posterior urethra showing lumen of urethra at top, vaginal epithelium below. Upper two-thirds is studded with glandular structures. ×26.

Fig. 21. A higher magnification of the glandular structures which are present in the section shown in Figure 20. ×68.

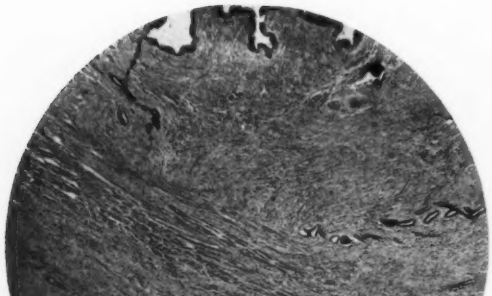

Fig. 22. Cross section of the same specimen taken at the neck of the bladder. Glands seen in mid portion on the right and in the upper left-hand corner. Urethra is above and vagina is below. ×26.

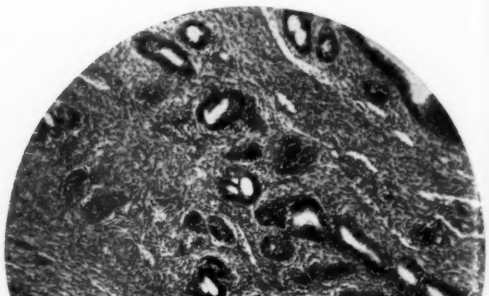

Fig. 23. Section through the prostate of a newborn male. ×67.

The urethra never seems to retain a constant shape or assume a definite position in all specimens. It is noted in Figure 7 what an odd shape it may attain. Here there are many finger-like projections of the urethra extending in different directions dividing the urethral wall into nine folds. This is a good instance to show how longitudinal sections might easily confuse an investigator. In a cross section of an intact urethra, all outpouchings are immediately identified at a glance. There are no epithelial remnants below the mucosa, and there are no glandular structures seen. However, there is a small nest of epithelial cells seen just to the right of the second upper vertical projection in the upper center of the photomicrograph. This is a so called von Brunn nest since it has no connection with the lining epithelium.

In 1 case a lymphocytic infiltration has been seen about the urethra. This is well demonstrated in Figure 8. The fold in the extreme right hand side of the lumen is heavily infiltrated with lymphocytes. This was in a newborn who had lived for 5 days. The crista urethralis is well outlined.

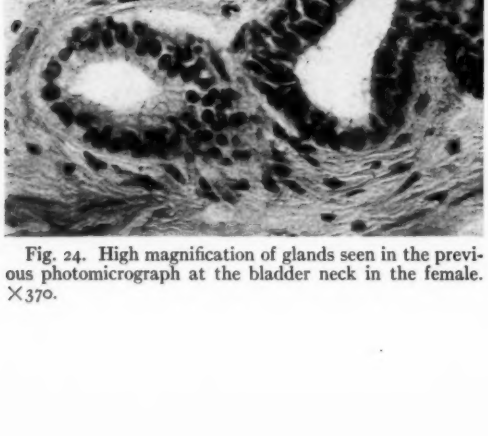

Fig. 24. High magnification of glands seen in the previous photomicrograph at the bladder neck in the female. ×370.

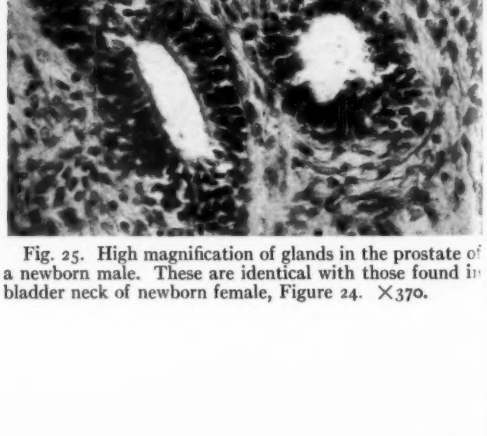

Fig. 25. High magnification of glands in the prostate of a newborn male. These are identical with those found in bladder neck of newborn female, Figure 24. ×370.

The photomicrograph shown in Figure 9 from posterior urethra of Case 21 is shown here to have the reader appreciate how different this is from all others seen. It is noticed at a glance that there are many glandular structures seen about the urethra. Some of these structures in the immediate vicinity of the urethra are seen emptying into it when studied in serial sections. These structures near the urethra are lined by transitional epithelium. Some contain keratin and squamous cells but most of them do not. Here, too, at a glance the extent of these structures is seen and the muscular wall of the urethra is well outlined. There is a large group of glandular structures seen in the lower left-hand corner. These are lined by columnar epithelium with clear cytoplasm. These glands rest on a bed of striped muscle. They cannot be considered folds or epithelial nests and by studying the serial sections they are found to end blindly.

A polypoid growth was seen in the urethra in only one specimen. A schematic drawing of this growth is shown in Figure 10. This was one of the specimens in which an incision had been made through the roof in order to lay out the urethra. The growth was seen macroscopically arising from the crista urethralis. No other abnormality had been seen in this specimen. The growth occupied the entire posterior urethra and the planes of section described in this paper are shown at *A*, *B*, and *C* respectively. A cross section taken through *A* is shown in Figure 11. It demonstrates a layer of cavernous tissue in the submucosa and at the base of the polypoid growth. A small intraepithelial glandular structure is seen at *G*. No other abnormalities are seen microscopically and no other glandular structures make their appearance. A cross section through *B* (Fig. 12) is taken to show where this polypoid growth leaves the mucous membrane of the urethra. A section through *C* (Fig. 13) is taken closer to the bladder and here, too, there are no glandular structures. It will be noted that cavernous tissue is seen in all sections. The intraepithelial gland seen at *G* extends throughout the greater part of the posterior urethra without altering its size or position. A very high magnification of the polypoid growth is shown in Figure 14. It consists almost wholly of the connective tissue. It might be well to add that this specimen was obtained from a 2 day old infant who died of congenital heart disease. This growth was quite prominent to the naked eye in the gross specimen and when compared to the small lumen of a newborn female urethra it assumes gigantic proportions. It is quite obvious how easily such a structure may cause an impairment of the normal urinary stream. Microscopic findings of this tissue are entirely in keeping with those of G. Thompson who studied pieces of tissue resected from the bladder necks of 24 females who had been suffering from partial urinary obstruction. As in his cases, no evidence of glandular tissue was found in the substance of the removed tissue.

The next specimen is from Case 19 in which a huge cyst was found in the lateral aspect of the floor of the urethra (Fig. 15). The length of the urethra from the meatus to the bladder neck in this specimen measured 18 millimeters. The proximal 7 millimeters was embedded in paraffin and sectioned in the usual manner every 6 micra beginning at its distal end and proceeding toward the bladder. In the first 75 sections, a hyperplasia of squamous epithelium could be seen in the urethra together with several outpouchings of its epithelial lining. The mucous membrane in several instances showed intraepithelial vacuoles filled with keratin-like substance. In several places desquamated keratin was seen in the lumen of the urethra.

In the 75th section, or approximately 0.4 millimeter from the distal end of this embedded specimen, several small glandular structures appeared in the lateral part of the specimen. These were deeply embedded in the musculature of the urethra and assumed a lateral and caudal relationship to it. Each gland was lined by definite columnar epithelium with clear cytoplasm and typically flattened basal nuclei. Each individual section was carefully studied and the glands were seen to fuse as the bladder was approached. This appeared about 125 micra from its origin. The photomicrograph in Figure 16 clearly shows it with its relation to the urethra at *A*.

It may be well to note here that the urethra assumed an elongated, flattened appearance with one end turned up and the other down. There were several small outpouchings of the mucosa. As the study was carried out toward the bladder this glandular structure increased tremendously in size, out of all proportion to the growth of its neighboring glands. Its lining epithelium then began to take on the character of stratified squamous epithelium with an unusually heavy layer of squamous cells. This is well seen in Figure 17.

The innermost layers of these squamous cells became detached and desquamated into the lumen of the gland. The lumen in turn rapidly became packed with desquamated cells and keratin. Glandular epithelium was no longer seen in its lining membrane. As this structure increased in size it incorporated all its neighboring glands, ruptured their walls and incorporated them into the one structure (Fig. 18). This occurred in much the same manner as a large drop of mercury incorporates its neighboring small droplets. In this way this newly formed cyst became larger and larger at the expense of its neighboring glands and it was soon packed with keratin and desquamated cells. It assumed a spheroidal shape with distended walls as if under pressure of the packed keratin in its lumen. The cyst became broadest in diameter about $^1/_5$ millimeter from the neck of the bladder. It occupied the entire posterior urethra and, at no point, did it ever communicate with the urethra itself. In one part of the specimen it was separated from the urethra by just a few strands of connective tissue. The structure ended before the neck of the bladder was reached.

As has been stated previously only every fifth slide had been stained with hematoxylin and eosin. This being an unusual finding, it was then possible to apply different stains at any given section. The mucicarmine stain was applied to several of these sections and 1 glandular structure is well illustrated taking the stain in Figure 19. Mucin takes a deep red stain which appears black in the ordinary black and white photomicrograph. The photomicrographs showing the relationship and size of the cyst suggest the greater pressure exerted on the cyst from within. Fortunately, this structure had not had its contents emptied spontaneously into the urethra or in the process of dissection.

What the explanation for the formation of this cyst can be is open for discussion. However, there have been many recent investigations on the effect of estrogenic substances which may shed some light on this problem. One explanation offered has been that the estrogens formed in the mother, pass on to the fetus through placental circulation, exert a specific action on certain epithelial structures. Squamous metaplasia of the prostatic urethra and the prostatic glands in the newborn has been well described by Brody and Goldman. Certainly there has been a change in the epithelial structure of this cyst from its definitely glandular beginning to its final keratinized stage. This may be a test application of a physiological reaction. It might be well to mention that a section taken at the broadest point of this cyst, gives this structure the identical appearance of a common sebaceous cyst. There are no secretory cells and the behavior of the epithelium is like that of squamous cells of low vitality. They degenerate and desquamate into the lumen.

In the light of these recent investigations on estrogenic effects in the offspring, it is pertinent to add that I have gone into the history of the mother of this infant of 4 weeks. She is a 33 year old Irish housewife who has never had a miscarriage or lues and there has been no history of endocrine disorder. Her menstrual cycle has always been regular and has been interrupted only by this first pregnancy.

A cross section of a posterior urethra of a full term infant who lived for 3 days is shown in Figure 20. Here at a glance one can see glandular structures studded throughout the upper two-thirds of the photomicrograph. The urethra is seen in the upper portion and the vagina below. Orientation here is easy and the lowermost glands are seen lying on a bed of striated muscle. The striated muscle is well brought out with the phosphotungstic-acid hematoxylin stain. The glandular structures in the upper portion of the figure are lined by modified transitional epithelium.

Serial sections show some of these communicating with one another. Only the large one just beneath the urethra communicates with the urethra and no others communicate with it or with the urethra. A high-power magnification of the structures seen lying adjacent to striated muscle is shown in Figure 21. Here the glandular nature of the structure is definite. They are lined by epithelium. A study of the sections was carried out into the bladder neck and trigone. Here, at the bladder neck, these definite glandular structures are still seen (Fig. 22). They are very deeply embedded and lie almost half way between the vagina and the urethra. These structures are shown in Figure 24 at a magnification of 370. The tall columnar epithelium with clear cytoplasm is distinct. The mosaic tile appearance of the cytoplasm in one of these glandular structures at left is due to the fact that the section was cut tangentially.

The prostate of a newborn full-term male was then sectioned for comparison with the structure of the glands found in the posterior urethra of the female. Figure 23 shows glandular structures which are indistinguishable from those seen in Figure 21 under the same magnification and belonging to the female posterior urethra. At a magnification of 370 this same section of the male prostate is shown in Figure 25. In comparing this photomicrograph with that of the same magnification seen in Figure 24 it would be very difficult indeed to tell which was prostate and which was gland at the bladder neck of the female.

SUMMARY

There has been much difference of opinion among urologists as to whether the female urethra contains glands in its proximal third. On the one hand, F. P. Johnson, A. I. Folsom, and M. J. Renner have found glands in a large proportion of females. On the other hand, McKenzie and Beck and Cabot and Shoemaker have studied the proximal urethra thoroughly in more than 109 routine postmortem examinations taken in all decades of life and have found no evidence of glands in this region. Because of these widely varying opinions we decided to study the proximal urethra in a series of newborn infants because these specimens would resemble the normal more than would specimens from later decades of life after there had been opportunity for intercurrent pathological processes. In 2 cases of 24, glands indistinguishable from those in the infantile male prostate were found. At first the study was made by cutting longitudinal sections but after we had made 7 such sections it became plain that folds and furrows also running longitudinally became confusing, and we therefore adopted the invariable method of sectioning the urethra transversely with all walls of the urethra intact. In our sections the most constantly present fold in the proximal urethra was the crista urethralis. We found, also, that there was a layer of erectile tissue in the submucosa, varying widely in thickness.

Since it is not at once apparent to the general reader what could be the clinical implications of the foregoing neutral morphological facts, some such implications might well be mentioned. We have shown some additional evidence that in less than 10 per cent of cases a rudimentary female prostatic structure exists, and that the glandular elements of this structure penetrate down to the sphincter muscle, sometimes occupying the cephalic two-thirds of the urethrovaginal septum. Consequently, some females can have urinary obstruction because of hypertrophy of these glands, with or without infection. In 1 instance we found a large cyst on the floor of an infantile proximal urethra, of glandular origin with squamous metaplasia. If in later life such a cyst had ruptured into the urethra during labor or from erosion incident to infection, it would have been diagnosed as an anatomical diverticulum.

CONCLUSIONS

This study of posterior female urethra is based on material taken from 21 full term infants and 3 seven-month premature infants. Cross sections are demonstrated as being superior to longitudinal sections in such a study.

1. Only 2 specimens showed definite glandular tissue indistinguishable from those of the prostate in the newborn male, 21 failing to show any such structures.

2. A huge cyst of glandular origin which had undergone squamous metaplasia, probably on the basis of estrogenic stimulation, was found in 1 case.

3. A polypoid growth was seen in 1 instance.

4. The female urethra is embedded in cavernous tissue.

5. The crista urethralis is the most constant and prominent fold of the female urethra.

6. Glandular structures usually disappear from posterior female urethra before the 7th fetal month as shown by the fact that none of the premature specimens showed glandular structures in the posterior urethra, though only 3 such cases were studied.

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THE PATHOLOGY AND TREATMENT OF INDOLENT ULCERS OF THE LEG

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IN spite of an improved understanding of the varicose vein syndrome, certain fundamentals have frequently been overlooked or misinterpreted. In particular, the problem of the treatment of varicose ulcers has been made difficult by lack of recognition of the underlying pathology, and by the fact that these lesions have often been confused with certain other types of ulcerations of similar appearance.

The aim of this paper is to throw light on the various elements of the problem and to indicate the channels which therapy should logically follow. Observations are presented on the common etiological factors in related types of indolent ulcers and their effect on the healing process.

ETIOLOGY AND PATHOLOGY OF CHRONIC ULCERATIONS OF THE LEG

Indolent ulcers of the leg, whether associated with varicose veins or not, have certain characteristics in common. They are chronic necrotizing lesions which not only fail to heal spontaneously but usually become larger. They are most often situated in the lower half of the leg or around the malleoli, and appear in the center of an area of discolored and indurated skin. The edges of the lesions are rounded, fairly regular in contour and not undermined. The ulcer base is gray-yellow in color and from it is secreted a rather profuse seropurulent fluid having a characteristic disagreeable odor.

Such lesions represent the effect of a *nutritional* deficiency on the functions inherent in cutaneous cells. Defense mechanisms, reproduction, and growth, are impaired because of an ischemia arising from peripheral, arterial, or venous disturbances. This, therefore, is a disease peculiar not only to the varicose state, but to any condition of the skin in which there is a reduced blood supply. In some cases, a decreased cardiac output may exert a further inhibiting effect.

The skin of the lower leg and ankle is particularly vulnerable to such disturbances because of the exposed location, poor protective padding over bony prominences, and a relatively meager arterial supply (Bellocq, quoted by Meisen). These factors make this region susceptible to occlusive arterial disease, trauma, or any phenomenon which may compress the subcutaneous vascular bed. Occlusive arterial lesions generally involve the whole extremity and produce a diffuse effect on the skin, while trauma or disturbances arising in veins are apt to lead to more localized changes. When more than one of these factors is present a particularly disabling lesion may develop.

Varicose indurations represent only one form of this disease. Microscopic examination of areas of this type shows atrophy of the epidermis with hyperkeratosis, loss of the rete pegs, and destruction of the hair follicles. The subcutaneous tissue is replaced by a thick layer of fibrous connective tissue containing many clumps of hemosiderin. There is a perivascular infiltration of lymphocytes and plasma cells. The blood vessels are few in number and compressed by scar tissue (Bancroft and Stanley-Brown). This fibrous scar, by choking off the circulation, inhibits cell repair, and when the skin in such an area is traumatized, bacterial invasion promptly leads to necrosis and loss of epidermis. Organisms ordinarily of low pathogenicity are able to effect this destructive process, and since healing is impeded or prevented by the nutritional state, a slowly enlarging chronic sore results.

The mass of subcutaneous scar tissue is of basic importance and is considered by many to be the result of passive congestion and

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chronic edema. However, Zimmerman has shown that the fibrosis is more likely inflammatory in origin and he presents the following evidence:

1. The long axis of the patch is usually parallel to the varix and in many instances the varicosity may be palpated as a groove or channel passing through the board-like area. Infra-red photography bears out this relationship.

2. No parallel exists between the extensiveness of the varicosities and the severity of the skin lesions. One may find extensive ulceration with small varices; and conversely, tremendous dilatations without evidence of skin involvement.

3. The area of involvement does not lie in the most dependent portions where congestion would be most severe.

4. The lesions are sharply circumscribed, which fact would be difficult to explain on the basis of chronic congestion.

5. Long standing chronic passive congestion is not associated with indurations of this sort.

If one is to accept these arguments, it appears logical that phlebitic inflammatory disease forms the basis of varicose indurations and ulcers. Similarly, other localized subcutaneous fibroplastic processes may lead to a circulatory deficiency of the skin, as is commonly seen following inflammatory lesions of the deep veins. How a deep phlebitis extends to involve the subcutaneous structures is still unknown. It is assumed that the process utilizes the dilated communicating veins (which are most numerous in the lower third of the leg where involvement is prone to occur) to extend outside the crural fascia. The presence of chronic capillary stasis and edema does not appear to be a primary etiological agent but probably contributes to the delayed healing of ulcers.

Local scarring may occasionally result from trauma, particularly when there is a comminuted fracture of the lower leg or ankle. Such fractures are apt to injure and thrombose the major venous trunks. In addition, the vascular bed of the skin may be damaged or a large subcutaneous hematoma may form and when organized produce a dense scar mass, so that the cutaneous circulation becomes impaired. The end result is a typical circumscribed area of discolored, brawny, and atrophic skin. Ulceration is likely to follow, and such ulcers progress along the same course as varicose lesions.

Once ulceration has occurred, another factor, secondary infection, is introduced. Microorganisms, by stimulating defense mechanisms, further increase the amount of scar tissue present. Long standing ulcers become centered in an area of skin having an almost cartilaginous consistency, and an area involved in recurrent ulcerations tends to become more atrophic and malnourished with each attack.

Besides the factor of local scarring, other less understood elements may be involved. Obesity is a frequent complication which impedes healing. This effect may be due to hypothyroidism in some, though many of these individuals have metabolic rates within normal limits.

The effect of patent and incompetent varicosities on cutaneous nutrition is thought to be of importance only when there is marked impairment of the circulation from periphlebitic scarring. The few narrowed channels which pass through the scar are able to carry only a limited amount of blood because of, first, the mechanical obstruction and, second, the stasis and trauma produced by forces transmitted peripherally through the varices. This latter effect is ordinarily of small importance since it is spread over a wide area of capillaries, but, when in combination with other circulatory deterents, its influence is amplified.

The obliteration of varicose veins or the use of supportive bandages leads to the healing of ulcers because both forms of treatment tend to prevent distal capillary damage from pressure surges and venous stasis. These measures are, therefore, of value because they remove some of the load on the vascular bed and allow a more normal flow of blood. Further investigation is needed on this particular phase of the problem.

To summarize the types and factors involved in the production of indolent ulcers, the following outline is included:

I. True varicose ulcers—the result of a phlebitis arising in superficial varicosities.

II. True varicose ulceration plus some other factor:

A. Cardiac disease with decreased peripheral blood flow.

B. Occlusive arterial disease: (1) Senile arteriosclerosis, (2) Diabetic arteriosclerosis, (3) Luetic arteritis, and (4) Thromboangiitis obliterans.

C. Occlusive or inflammatory venous disease: (1) Thrombophlebitis of the deep veins, and (2) Thrombosis or obstruction of the deep venous trunks from fractures about the ankle and leg.

D. Functional venous disease—impairment of muscular activity (and of the pumping action) due to ankylosis of the knee and ankle joints.

E. Obesity—this mechanism is not clear.

F. Mixed types.

III. Chronic ulceration due solely to one of the factors listed under II, and totally dissociated from varicosities.

THE QUANTITATIVE EFFECT ON HEALING OF FACTORS MENTIONED

It is evident that organic and functional arterial and venous lesions may profoundly influence the healing of infected cutaneous wounds of the leg. The type and magnitude of the effect may be demonstrated by applying a standard method of treatment to different cases and measuring the trend and rate of healing from week to week.

Materials and methods. All patients were treated with weekly applications of either the Unna's paste boot or the elastic adhesive bandage because of its effectiveness, ease of application, and low cost.

Both kinds of dressing act as a supporting layer of "investing fascia" around the superficial veins and thus improve the aspirating action of muscular activity so that the veins are emptied more effectively. In addition, varicosities are prevented from becoming distended with large pools of stagnant blood. Locally, the bandage acts as a protective coat to prevent injury to delicate proliferating capillaries and epithelial cells, and by its glove-like action compresses and suppresses exuberant granulations. Douglas suggests that the elastic adhesive bandage serves a specific purpose in that it tends to draw the wound edges together, narrowing the defect.

The elastic adhesive has one disadvantage: some individuals are allergic to the adhesive mass. Of the last 100 cases treated with this dressing, 3 developed a true allergic dermatitis. This is not to be confused with the type of rash that appears under overlapping folds of the bandage and which is due to the application of the bandage with unequal tension. Should a true sensitivity be manifested, treatment is changed to the boot, which does not cause a cutaneous reaction. The boot,[1] however, is not so efficient as the elastic adhesive and presents problems in application.

Local medications are considered of minor value. Anderson stressed the relative unimportance of local antiseptics in healing infected wounds as against general measures designed to increase tissue immunity. His experiments showed that antiseptics were generally ineffective in the presence of tissue necrosis and that delayed repair occurred when there were specific types of infection, necrotic tissue, or inadequate drainage. The presence of large numbers of organisms on the surface of the wound did not retard healing.

All types of local application have been tried on ulcers and little or no difference was noted in the healing rate of different groups. We have, however, used certain preparations for specific effects: anesthetic ointments were used on painful ulcers, and either 2 per cent aqueous solution of gentian violet or powdered crystalline sulfathiazole was applied for their astringent and bacteriostatic action. This reduces the amount of exudate and eliminates the odor.

Records of the progress of healing were obtained by tracing the outline of the ulcers on cellophane each time the dressings were changed—over 600 such tracings were made. These were later transferred to paper record sheets, and the ulcer areas determined with the aid of a planimeter (method of Carrel and Hartman). It is realized that this is not the ideal method because it neglects the third dimension of the wound; i.e., depth. Yet when surface area is plotted against time, a curve is produced which adequately represents the trend of the particular lesion. By comparing lesions involving different factors with simple varicose ulcers, one may determine the effect exerted by these elements. In addition, calcu-

[1]Boots, when used, were applied according to a method used at the Northwestern University Clinic.

TABLE I.—HEALING RATES OF INDOLENT ULCERS TREATED WITH SUPPORTIVE BANDAGES

Type of case	Type of bandage	Number of ulcers in each group	Average initial size in sq. cms.	Average number of weeks until completely healed	Average rate of healing in sq. cms. per week	Calculated rate of healing in sq. cms. per week (with elastic adhesive) of a simple varicose ulcer of similar size
1. Simple varicose ulcer	Elastic adhesive	14	4.0	5.6	0.9	
		10	8.5	6.5	1.4	
		3	23.2	7.0	3.4	
	Unna's boot	10	3.8	6.5	0.4	
2. Ulceration following a deep thrombophlebitis	Elastic adhesive	3	3.0	7.0	0.13	0.7
		4	4.5	24.0	0.65	0.9
3. Varicose ulcer plus the factor of obesity	Elastic adhesive	5	3.9	19.6	0.26	0.8
4. Varicose ulcer plus arteriosclerosis	Elastic adhesive	1	2.4	7.0	0.31	0.6
		1	7.7	33.0	0.33	1.3
		1	15.9	33.0	0.48	2.4
5. Mixed types: a. Varicose ulcer, arteriosclerosis, and comminuted fracture above ankle	Elastic adhesive	1	4.6	28.0	0.17	0.9
b. Varicose ulcer, arteriosclerosis, and obesity.		1	1.3	7.0	0.19	0.4
c. Ulceration after deep phlebitis, and obesity		1	5.4	10.0	0.54	1.0
6. Chronic ulceration associated with fractures (no varices)	Elastic adhesive	1	2.3	6.0	0.38	0.6
		1	4.1	6.0	0.68	0.8

lations of the rate of healing, square centimeters per week, for the total periods involved in repair yield an index of the effectiveness of the treatment used. A gauge is thus established which may be used to evaluate various forms of therapy. Cases selected are representative of the factors under consideration. Table I includes a summary of results.

The simple varicose ulcer. A total of 37 such cases was studied; 27 patients were treated with elastic adhesive bandages and 10 with Unna's boots. These ulcers varied in duration from 1 to 78 weeks, the average being 20 weeks. The associated varicosities were either 3 or 4 plus dilatations[1] and all incompetent.

The ulcers treated with elastic adhesive were all healed within 9 weeks, though one was closed as early as 3 weeks after the commencement of treatment. The curves of healing for this group of cases show a symmetrical trend not unsimilar to that observed by Douglas and Anderson.

A comparison of the healing in these 27 cases with the calculated time necessary for complete healing of defects of similar size in normal skin is of interest (Table II). The formulas of Du Nouy were used in making the calculations. Fifteen ulcers healed less rapidly than defects in the normal skin with an average of about 2 weeks' delay. Seven ulcers were healed at the same time as the theoretical lesions, and 5 healed more rapidly (about 2 weeks faster). These figures indicate that the influence of the pathological processes involved in the production of ordinary varicose ulcers is relatively small and easily overcome by the use of elastic adhesive plaster. Once the inhibitory factor is reduced to the point where cell repair is possible, proliferation proceeds at about the *normal* rate.

In order to establish a standard which could be used to determine the effect of various etiological elements, these cases were divided into 3 groups: those ulcers smaller than 6.45 square centimeters, those between 6.45 and 13 square centimeters, and those between 13 and 24 square centimeters. This is necessary because the initial size of the lesion is important in determining the rate of healing since Carrel and Hartman, and Du Nuoy have shown that large wounds heal more rapidly than smaller ones. Such grouping also in-

[1]Varices are roughly graded from 1 to 4 plus, 1 plus being the minimal size seen and 4 plus the maximal.

creases the significance of the average figures. There were 14 cases in the first group, 10 in the second, and 3 in the last.

Determination of the healing rates indicated that an average lesion of 4.0 square centimeters healed at a rate of 0.9 square centimeter per week. Ulcers having an initial average size of 8.5 square centimeters healed at a rate of 1.4 square centimeters per week, and those of an initial size of 23.2 square centimeters healed at a rate of 3.4 square centimeters per week. These velocities represent the average of healing rates calculated for the total period necessary for complete healing of the ulcer.

The 10 patients treated with the boot healed within 14 weeks, the earliest one closing at 4 weeks. These had an average initial size of 3.8 square centimeters and healed at a rate of 0.4 square centimeter per week. This is a rate somewhat slower than that obtained with elastic adhesive and would indicate that the boot is a less efficient form of therapy.

Ulceration following a deep thrombophlebitis. Homans (1917) first differentiated this type of lesion from the ordinary varicose ulcer and showed that they appear from 1 to 20 years after a phlebitis of the deep veins. In these cases the usual therapy is very slowly effective and often fails. Seven cases in which healing was finally completed are included to illustrate the slow rate of closure. These were typical cases all of which exhibited the usual ulceration and incompetent saphenous varicosities. All were treated with elastic adhesive. Their healing curves show a very slow rate of epithelization which progressed irregularly with considerable variation from week to week. Three ulcers having an average initial size of 3.0 square centimeters healed at an average rate of 0.13 square centimeter per week. Four other ulcers having an average initial size of 4.5 square centimeters healed at an average rate of 0.65 square centimeter per week. These figures will be discussed later.

Varicose ulcers plus obesity. It has been noted that varicose ulcers in obese patients heal more slowly than in slender people. Five cases are presented here to show this effect. Body weights varied between 220 and 260 pounds. Healing was again noted to proceed irregularly and at an average rate of only 0.26 square centimeter per week. The average size of the lesions was 3.9 square centimeters.

TABLE II.—A COMPARISON OF THE HEALING TIME, IN WEEKS, OF 27 SIMPLE VARICOSE ULCERS.

Ulcers that healed less rapidly than defects in normal skin (15 cases)		Ulcers that healed in the same time as defects in normal skin (7 cases)		Ulcers that healed faster than defects in normal skin (5 cases).	
Calculated time of healing of defects in normal skin	Actual time of healing of ulcer	Calculated time of healing of defects in normal skin	Actual time of healing of ulcer	Calculated time of healing of defects in normal skin	Actual time of healing of ulcer
3	4	3	3	7	5
3	4	4	4	9	5
3	5	4	4	9	8
3	6	5	5	10	9
4	5	6	6	11	9
4	5	7	7		
4	5	7	7		
4	5				
4	7				
4	7				
4	9				
5	6				
5	6				
5	7				
6	7				
Average: 4	6	5	5	9	7

Varicose ulcers plus arteriosclerosis. Patients past the fifth decade of life respond more slowly to treatment because of decreased peripheral flow of blood and decreased metabolic activity of the body cells. Three patients were selected to show this effect. They were 62, 68, and 70 years of age and had advanced arteriosclerosis as indicated by pipe stem, beaded, radial and anterior tibial arteries. Peripheral pulse beats were absent or diminished. In the first patient there was a varicose ulcer 7.7 square centimeters in size which healed at a rate of 0.33 square centimeter per week. The second patient had an ulcer with an initial size of 15.9 square centimeters which healed at a rate of 0.48 square centimeter per week; the third had an ulcer with an initial size of 2.4 square centimeters

which healed at a rate of 0.31 square centimeter per week.

Ulceration induced by trauma. Fractures of the leg and ankle may so disturb the circulation that healing of cutaneous lesions is inhibited. Two cases illustrate this.

W.D., 50 years old, had a compound both-bone fracture in the middle third of leg 10 months before admission. An ulcer remained at the site of the skin perforation over the crest of the tibia and was surrounded by the typical phlebitic induration which involved the lower two-thirds of the leg. Initial size of lesion was 4.1 square centimeters and the rate of healing 0.68 square centimeter per week.

H.J., 57 years old, broke his leg above the ankle 40 years prior to admission. Since this injury the ankle and foot swelled whenever he was up and around. During the last 10 years the skin over the lower half of the leg became increasingly indurated. Two years ago an ulcer appeared. When first seen this measured 2.3 square centimeters; it healed at a rate of 0.38 square centimeter per week.

In both these patients there was no evidence of venous dilatation.

Several factors combined. Where several of these conditions are involved, healing is almost always very slow and irregular. Three cases illustrate this.

One patient had a varicose ulcer plus comminuted fracture of the ankle and advanced arteriosclerosis. Initial size of the ulcer was 4.6 square centimeters and it healed at a rate of 0.17 square centimeter per week.

There was an ulcer following deep thrombophlebitis in a very short, obese patient weighing 245 pounds. Initial size of the ulcer was 5.4 square centimeters; it healed at a rate of 0.54 square centimeter per week.

Another patient had a varicose ulcer, incompetent veins, plus obesity (220 pounds) and arteriosclerosis. Initial size of the ulcer was 1.3 square centimeters; it healed at a rate of 0.19 square centimeter per week.

No response to supportive bandages. In some patients when multiple inhibiting factors are present, the use of supportive bandages does not result in satisfactory healing. A brief summary of 4 cases will demonstrate this.

J.Z., age 50, weighed 220 pounds. The patient had a fracture and extensive deep thrombophlebitis. Thirty years before admission the middle third of the left tibia was fractured. Three years prior to admission, he developed a lobar pneumonia complicated by an extensive deep thrombophlebitis of the left leg. While he was still in the hospital an ulcer appeared over the site of the old fracture. This ulcer enlarged rapidly and on first admission was 107.3 square centimeters in area. There was a dense, brawny, encircling induration extending from the knee to the ankle. Elastic adhesive bandages and local applications of gentian violet were used and after 20 weeks the ulcer was reduced to 46.6 square centimeters. In spite of continued therapy there was no further improvement for the next 20 weeks. Sponge pressure was then applied, and with this the ulcer enlarged to 64.5 square centimeters. This was discontinued after 12 weeks and sulfathiazole powder applied locally under the adhesive bandage; still the ulcer continued at about the same size and after a total of 84 weeks of treatment measured 59.5 square centimeters. The patient was then advised that skin grafting and a modified Kondoleon operation were necessary. He refused this aid.

F.B. was 62 years old. Deep thrombophlebitis with extensive ulceration and much scarring, plus cardiovascular syphilis, were present. Fifteen years prior to admission he developed a cellulitis of the left foot. The infection led to a thrombophlebitis which was followed within a few months by the appearance of an ulcer in the middle third of the leg. He had had a 4+ Wassermann reaction for years and had received antiluetic therapy for irregular and intermittent periods. Five years ago systematic and adequate therapy was started and has been continued to the present time. When first seen the ulcer measured 37.7 square centimeters. Elastic adhesive and gentian violet were applied at weekly intervals. Sixteen weeks later the lesion was 14 square centimeters in area and continued about this size for the next 20 weeks. He dropped out of the clinic for the next 20 week period and returned with a lesion 65.4 square centimeters in size. He was again placed on the above medication and after 16 weeks has remained *in statu quo*.

A.Z., 65 years old, had 2 varicose ulcers with extensive local scarring and advanced arteriosclerosis. Ulcer on right leg was 4.4 square centimeters in size, of 20 years' duration, and another on the left was 9.7 square centimeters in size, of 15 years' duration. One year prior to admission bilateral high and low saphenous legations were performed without affecting the course of the lesions. Elastic adhesive was used and after 40 weeks the ulcers were larger than at the onset (right, 16.5 square centimeters; left, 22.2 square centimeters).

A.H., 67 years of age, had a varicose ulcer, 21.3 square centimeters in size, of 8 years' duration. The patient was obese (220 pounds), had arteriosclerosis and extensive dense scarring from previous ulcerations. After 36 weeks' treatment the ulcer was reduced to 5.2 square centimeters. At this time all varices were obliterated with injections of sodium morrhuate. After 12 more weeks of elastic adhesive therapy the ulcer measured 4.0 square centimeters and since then has failed to become smaller.

In these cases healing was not complete after a year or more of therapy, and it is ob-

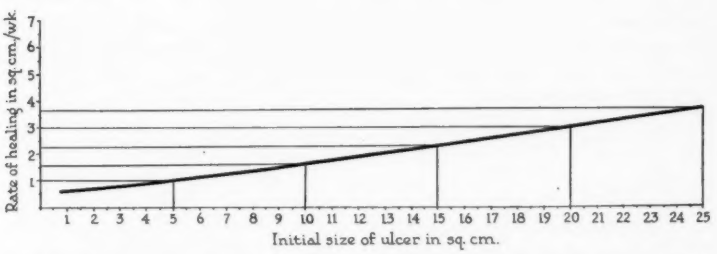

Fig. 1. The average healing rates of simple varicose ulcers, treated with elastic adhesive plaster, expressed as a curve. This graph indicates the relationship between the initial size of the ulcer and the velocity of healing.

vious that more radical therapy is indicated in such individuals. The further use of supportive bandages might eventually result in complete healing, though this is wasteful of both the patient's and physician's resources. In addition, long delayed healing is apt to be associated with excessive fibrosis which predisposes to recurrence of the ulcer.

A comparison of the healing rates of simple varicose ulcers with the more complex lesions indicates the degree of influence exerted by the complicating elements. Given a simple ulcer of a certain size, one is able to predict its healing rate with the use of Figure 1. When this rate is compared with the observed velocity of healing of a complicated ulcer of similar size, it is noted that, in the latter type, there is a definite prolongation in the healing time. The last column of Table I lists these calculated velocities and shows that the healing may be from 1.4 to 6 times slower in the complex type than in the simple lesion. Slowest rates were observed in those ulcers associated with disease of the deep veins or advanced arteriosclerosis. This observation lends support to the concept that circulatory disease is of basic importance in the formation of indolent ulcers.

A LOGICAL PLAN OF TREATMENT

The pathological pattern should be the basis for the selection of therapeutic measures. This calls for the analysis and treatment of systemic conditions, as well as local ones involving only the legs. Such a survey may include examination of the cardiovascular system as a whole, estimation of the protein and vitamin levels, and a check of the total caloric intake. In the obese patient, dietary restrictions and planned weight reduction should be enforced.

Successful treatment of lesions associated with arterial disease depends on the types and degree of involvement. In patients in whom arterial damage of a mild or moderate degree is present, it may be worth while to try such measures as mechanical intermittent venous occlusion, the application of radiant heat, and the use of dilator substances such as prostigmine or intravenous typhoid vaccine. Small doses of thyroid may occasionally be used to increase the cardiac output and stimulate metabolism.

Venous disturbances, which are present in most cases, are treated with supportive bandages. When local infection is under control, varicosities are obliterated by injection or ligation. These measures will heal the great majority of ulcers. However, if healing is delayed, more radical methods should be instituted.

Should the bandages fail to promote healing, some operative procedure is indicated. This circumstance is commonest in those ulcers associated with a deep thrombophlebitis. Surgical therapy is of 3 types: measures used to occlude incompetent varices, fascial stripping operations, and skin grafting. Linton and Keeley have combined skin grafting and ligation of the saphenous trunks and communicating veins. The results have been good, yet the method is quite extensive and does little to directly improve the cutaneous blood supply. The obliteration of incompetent veins exerts an indirect effect but does not overcome the obstruction to circulation

induced by the fibrous deposits. More appropriate is some procedure such as complete excision of the induration with grafting, or a modified Kondoleon operation which removes the dense subcutaneous scar and investing fascia. These methods make possible a new ingrowth of capillaries.

If very large ulcers are present, there is a prolonged period of disability which may be shortened by skin grafting. New skin may be applied directly to the ulcer bed (Smith) or implanted into a defect created by excision of the whole indurated area (Douglas). This latter procedure is most valuable because the scarred region is removed, allowing the ingrowth of blood vessels sufficient to maintain the vitality of the implant and prevent breakdown. This method is the one which is followed by us whenever possible.

A METHOD FOR THE EVALUATION OF OTHER MODES OF THERAPY

It is suggested that the healing rates of simple varicose ulcers, treated with elastic adhesive bandages, be used as a gauge to test the efficiency of other forms of therapy.

Such a comparison may be made in the following manner: The initial size of the test ulcer is determined with a cellophane tracing and planimeter. The area is divided by the number of weeks needed for complete healing, to yield the total healing rate. This is then compared with the velocity of repair of a lesion of similar size, as indicated in Figure 1, to note which treatment promotes most rapid healing.

A series of such determinations would result in a quantitative evaluation of the effectiveness of the newer therapeutic measures.

SUMMARY

The underlying basis of indolent ulcerations of the leg is depicted as a nutritional deficiency, or ischemia resulting from local cicatricial changes. These fibrous deposits may arise because of venous and arterial disease processes or directly from trauma to the cutaneous blood supply. The usual types of chronic ulcerations are outlined with discussion of the various elements involved.

A quantitative study of the effects of these factors is presented in order to clarify the rôle played by each and to indicate the effectiveness of elastic adhesive plaster in the treatment of ulcers.

Suggestions for treatment are offered and a gauge (Fig. 1) is presented, with which one may predict the healing rate of a simple varicose ulcer of any given size, or which may be used to compare forms of therapy.

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THE EFFECT OF VARIOUS BLOOD SUBSTITUTES IN RESUSCITATION AFTER AN OTHERWISE FATAL HEMORRHAGE

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THIS study was undertaken to secure quantitative evidence concerning the value of the various blood substitutes in a hemorrhage which would be fatal if untreated. Many such substances have been tried in recent years, with conflicting reports regarding their merit. Beneficial results have been reported in which it was not shown that the experimental or clinical subjects would have died without such intervention. We have been unable to find any evidence pertaining to the therapy of traumatic shock or to the use of blood substitutes in which the recoveries observed could not be explained on the basis of chance or random sampling. The literature has been extensively reviewed recently (1, 2, 7, 15).

The reduction in blood volume is obviously the most important lethal factor in acute hemorrhage and, undoubtedly, is of major significance in traumatic shock. For its restoration many substances have been employed, including whole blood, plasma, serum, serum albumin, hemoglobin solution, red cell suspension, acacia, pectin, isinglass, methylcellulose, gelatin, and solutions of crystalloids. They have been tested by a variety of techniques which render uncertain their relative efficacy. Usually the experimental animals were subjected to general anesthesia; frequently hemorrhage was employed which was not shown to be fatal in itself, or was induced by the repeated withdrawal of small quantities of blood over a long period of time. The latter procedure affords little parallel to the clinical picture of hemorrhage as encountered in civil life or, more commonly, on the battle field; furthermore, the prolonged nature of this method involves complexities in the form of compensatory mechanisms which greatly increase the variability of the findings.

The present urgent need of a safe, adequate, and easily available medium for the replacement of lost blood volume led us to reinvestigate the problem. For this a uniform procedure was devised on the basis of which the individual blood substitutes could be evaluated.

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METHOD

Introduction. We chose to study resuscitation from a single massive hemorrhage (a) because only one factor, namely loss of blood, is initially involved, (b) because the extent of blood loss could be measured in regard to amount and duration of the hemorrhage, (c) because a large single loss of blood is the type of fatal hemorrhage which is most likely to occur in battle or civil life, and (d) because the use of blood substitutes has not been extensively studied after massive hemorrhage.

It should be emphasized that in most of the experimental and clinical work in which blood substitutes have been used the chief therapeutic interest has been placed on the treatment of shock. Shock has been produced usually by a procedure which has resulted in hemoconcentration and not in a significant loss of erythrocytes. Shock has also been produced by removing 100 cubic centimeters of blood in an anesthetized dog and repeating the hemorrhage at intervals usually of 30 minutes until the blood pressure has reached the "shock" level. Hemorrhage of this type is not common on the battle field or in clinical practice.

In interpreting the results obtained in this study, it is important not to confuse our results with those obtained when the blood substitutes were used to combat traumatic shock in which a severe loss of blood has not occurred. If a severe loss of blood has occurred, then we believe that the results of our study are directly applicable.

The method of bleeding and resuscitation. Using healthy dogs and local procaine anesthesia, we exposed one common carotid artery and external jugular vein. A large cannula was inserted into the artery for bleeding and another into the vein for giving the transfusion after hemorrhage. Bleeding was continued until the onset of acute "air hunger" or until respiration had ceased. At this time the flow of blood from the cannula had stopped or was flowing as infrequent drops. The

TABLE I.—CONTROL HEMORRHAGE SERIES

Dogs bled the maximum amount from one carotid artery without replacement

No. of dogs	Blood loss per cent	Lived	Died	Mortality per cent
7	45–49	1	6	86
8	50–54	2	6	75
14	55–59	2	12	86
14	60–64	2	12	86
7	65–	1	6	86
Totals 50	45–70	8	42	84 (Ave.)

TABLE II.—SALINE SERIES

Blood loss replaced by equal volume of 0.9% NaCl

No. of dogs	Blood loss per cent	Lived	Died	Mortality per cent
2	40–44	1	1	50
3	45–49	2	1	33
8	50–54	3	5	63
16	55–59	7	9	56
14	60–64	5	9	64
3	65–69	2	1	33
4	70–	1	3	75
Totals 50	40–78	21	29	58

blood flowed into a graduated cylinder, so its volume could be measured. The duration of the hemorrhage was recorded; it varied from 3 to 20 minutes. (It is known that bleeding from a large peripheral artery may cease after the blood pressure has been markedly reduced and time for the formation of a clot has occurred.)

When the hemorrhage had ceased, the artery was tied, and a volume of the blood substitute equal to that of the blood lost was injected into the jugular vein. The total time of the injection was about 5 minutes. The vein was tied, and the wound after treatment with sulfanilamide was closed. The animals were then observed for recovery for a period of 24 hours. Autopsies were performed in the case of death, the lungs being the chief organ inspected. Prior to death, when not immediate, blood was drawn for study of pseudoagglutination. This procedure was carried out on a series of 404 dogs, including a control group of 50 animals and similar groups in which the blood loss was replaced by saline, serum, citrated plasma, heparinized plasma, citrated whole blood, and special gelatin. Acacia and pectin were also tested; in their cases the animals were fewer in number, for reasons indicated below. All solutions were injected at body temperature and were free of insoluble matter.

RESULTS

I. Control group. A series of 50 animals were subjected to the procedure without replacement of the blood loss by a blood substitute.

Eighty-four per cent of the animals died after losing from 45 to 70 per cent of their total blood volume. The more detailed results are shown in Table I.

Comment. Since in a large group of experiments it is not feasible to determine the blood volume, the blood volume of each animal was calculated on the basis of the assumption that the blood volume is equal to 9.5 per cent of the dog's body weight. The dog's blood volume when measured by various methods (4, 6, 10) has been found to range from 6 to 10 per cent of the body weight. Allowing for the specific gravity of the blood as 1.055, the blood volume was calculated as 9.5 per cent of the dog's weight in grams. In the treated groups to follow, all animals from which 40 per cent of the calculated blood volume could not be obtained were discarded.

It is to be noted in Table I that on arranging the blood loss of the different animals in groups differing by 5 per cent, the mortality was the same in each group.

II. The normal saline series. In a series of 50 animals the blood loss was replaced immediately with an equal volume of 0.9 per cent sodium chloride in freshly distilled water (37° C.).

The mortality was only 58 per cent after a loss of from 40 to 78 per cent of the total blood volume (Table II). The majority of the dogs made an immediate but temporary recovery. Consciousness was generally regained at, or slightly prior to, completion of the infusion, and the animals were alert and walking within 5 minutes. Those that died usually became comatose and dyspneic after 2 or 3 hours and expired shortly thereafter.

Thus, the saline decreased the mortality from 84 (control) to 58 per cent. This difference is decidedly significant, since it is a difference which might occur by chance only in 5 out of 1000 groups of similar experiments in which 50 control and 50 treated animals were used.

Comment. That normal saline should be beneficial is not surprising in view of the following consideration. The animals after the massive hemorrhage still retained in their blood vessels from about one-half to one-fourth of their erythrocytes. It is known that patients with severe chronic anemia can live with 25 per cent hemo-

TABLE III.—SERUM SERIES

Blood loss replaced by an equal volume of serum prepared from defibrinated blood

No. of dogs	Blood loss per cent	Lived	Died	Mortality per cent
11	45–49	8	3	27
12	50–54	10	2	17
9	55–59	7	2	22
7	60–64	5	2	29
3	65–69	2	1	33
7	70–74	4	3	43
1	75–	1	0	0
Totals 50	45–76	37	13	26

TABLE IV.—GELATIN SERIES

Blood loss replaced by an equal volume of special gelatin in normal saline, adjusted to pH 7.4 with sodium bicarbonate

No. of dogs	Blood loss per cent	Lived	Died	Mortality per cent
2	40–44	1	1	50
6	45–49	4	2	33
4	50–54	2	2	50
16	55–59	9	7	44
9	60–64	7	2	22
10	65–69	4	6	60
3	70–74	3	0	0
Totals 50	40–74	30	20	40

globin value. So, if the erythrocytes could be kept in circulation until the circulation could compensate for an acutely decreased blood volume, then survival might be anticipated.

Hoitink subjected dogs to acute hemorrhage and tested various agents, and concluded that normal saline is superior to other blood substitutes or to blood transfusion. Most opinions are diametrically opposed to this; for example, Buttle, Kekwick and Schweitzer found saline to be totally ineffective in the treatment of hemorrhage in cats. The chief reason for such discrepancies is the failure of the investigators to use a sufficient number of animals so as to avoid errors due to chance or random sampling.

The failure to reduce the mortality to a value lower than 58 per cent was due, we believed, to the possibility that the sodium chloride was not kept in the circulation for an adequate period; it "leaked out" into the tissue.

With this idea in mind we next used dog serum as a blood substitute.

III. The serum series. Fifty animals were bled as before and were given an equal volume of pooled dog's serum prepared from defibrinated blood.

The mortality was only 26 per cent after losing from 45 to 76 per cent of the total blood volume. This result is so striking that a statistical testing of the significance is unnecessary (Table III).

Comment. It is obvious from the results that the serum was much better than the normal saline solution in resuscitating the animals. The serum, which does not leave the blood vessels, supported the circulation quite adequately by maintaining the blood volume.

IV. The use of gelatin as a blood substitute. Gelatin was first tested clinically by Hogan in 1917, but has never received a thorough trial, because other agents have been considered superior. Prejudice against gelatin has been based chiefly on its tendency to gel, its alleged antigenicity, the hazard of infection with anthrax or tetanus, and production of "intravascular clotting." Karsner and Hanzlik reported that solutions of gelatin, in common with other colloids, cause hemiagglutination.

Pseudoagglutination due to gelatin. When a purified gelatin (5 per cent in saline solution, pH 7.4) was given to dogs after an extensive hemorrhage, death occurred. When the blood was examined it was found to be dark brown in color. On shaking the blood it became bright red, but resumed the dark color again on standing a few minutes, during which time the erythrocytes sedimented rapidly. On examination the erythrocytes were found to manifest marked pseudoagglutination. It was observed that the intravenous injection of 10 per cent dextrose solution temporarily but markedly improved the condition of the dogs which were in coma with or without "convulsions." The dextrose solution, it was found, also decreased the sedimentation and pseudoagglutination *in vitro*, but this effect was not long sustained *in vivo*, since the dextrose concentration in the blood was not maintained.

After examining *in vitro* the effect of some 12 preparations of gelatin for their effect on sedimentation rate and pseudoagglutination, one preparation of gelatin was found which has less tendency than any of the others to cause this effect. It was decided to test this gelatin on a series of animals.

Favorable results with a special gelatin, U-17578. The gelatin was dissolved in normal saline to make a 5 per cent solution, the hydrogen-ion concentration of which was adjusted to 7.4 with sodium bicarbonate. The colloid osmotic pressure

TABLE V.—CITRATE PLASMA SERIES

Blood loss replaced by an equal volume of plasma containing 0.25% sodium citrate as an anticoagulant

No. of dogs	Blood loss per cent	Lived	Died at once	Died in 24 hours	Mortality per cent
4	40–44	0	4	4	100
9	45–49	2	5	7	78
10	50–54	4	3	6	60
12	55–59	5	2	7	58
8	60–64	3	5	5	63
1	65–69	0	1	1	100
4	70–74	1	2	3	75
2	75–	0	1	2	100
Totals 50	40–75	15	23	35	70

TABLE VI.—CITRATE AUTOTRANSFUSION SERIES

Blood treated with sodium citrate to concentration of 0.25% and reinjected

No. of dogs	Blood loss per cent	Lived	Died at once	Died in 24 hrs.	Mortality per cent
7	45–49	1	1	6	86
13	50–54	6	2	7	54
11	55–59	6	3	5	45
12	60–64	8	1	4	33
1	65–69	1	0	0	0
5	70–74	2	1	3	60
1	75–	1	0	0	0
Totals 50	45–83	25	8	25	50

of the 5 per cent gelatin was found to be the same as serum.

In a series of 50 animals the blood loss was replaced with an equal volume of the special gelatin solution. The mortality was 40 per cent. Thus, the gelatin solution was better, but not strikingly so, than the saline, since the difference observed, i.e., between 58 and 40 per cent, would occur by chance in 8 cases out of 100. However, the gelatin was obviously not so good as the serum.

Comment. We suspect that if an ashless gelatin could be found which has no tendency to cause pseudoagglutination of erythrocytes, it could be substituted for serum in emergencies. The repeated use of such gelatin, however, may not be found to be desirable, though it may be found to be less foreign to the body than pectin and acacia. A gelatin solution has the objection that it gels unless held at body temperature.

The antigenicity of gelatin is now considered to be negligible, and under present methods of preparation the possibility of bacterial contamination is so exceedingly remote that it cannot be considered to be a reasonable objection.

Unfavorable results with a special gelatin, "plasma gel." This gelatin was dissolved in normal saline to make a 5 per cent solution; it was not necessary to adjust the pH of the solution because it was 7.1 after the solution was made. A series of 10 animals were given this gelatin solution. The series was not enlarged because all 10 animals died, 6 rather promptly.

V. The citrated plasma series. Citrated plasma was used because we thought that it should prove to be better than serum. This anticipation did not prove to be true, however.

The plasma used was pooled from a number of dogs; it contained sodium citrate in a concentration of 0.25 per cent, which was the smallest concentration which would prevent the plasma from clotting.

Thirty-five of the 50 animals in this series died, 23 of them immediately (Table V). Those which died at once showed respiratory failure evidenced by a long period of apnea followed by isolated gasps. A few of the animals succumbed to ventricular fibrillation during the transfusion.

Comment. It is apparent from these findings that sodium citrate was toxic, although the material used was chemically pure. The toxicity of this salt is well known, and the amount given clinically in the usual transfusion is innocuous. The quantity required by our animals was in excess of the safe level in the majority of cases. When 0.25 per cent sodium citrate, dissolved in normal saline, was given rapidly to intact (nonbled) dogs in an amount equal to 60 per cent of the calculated blood volume, death resulted.

Lewisohn concluded that 1.5 grams was the fatal dose for an 11 pound dog and reasoned by analogy that 15 grams would be fatal for a 110 pound man. More recently Muirhead and others have called attention to the toxicity of sodium citrate when concentrated plasma is given. Our animals received on the average a dose of 1.0–1.25 grams for a 20 pound dog, or approximately 0.11 to 0.15 grams per kilogram body weight. This is between one-third and one-half the reported lethal dose for dogs which have not been previously subjected to extensive hemorrhage.

VI. Citrated autotransfused blood series. Citrated whole blood is frequently given in relatively large quantities to human subjects, without serious reactions. However, when such transfusions are given the citrated blood is generally introduced rather slowly. The rate of transfusion may account for the absence of toxicity or the presence

TABLE VII.—HEPARINIZED PLASMA SERIES

Blood loss replaced by an equal volume of plasma with 20 mgm. per liter of heparin as an anticoagulant

No. of dogs	Blood loss per cent	Lived	Died	Mortality per cent
15	45–49	14	1	7
14	50–54	14	0	0
7	55–59	6	1	14
9	60–64	8	1	11
2	65–69	2	0	0
2	70–74	2	0	0
1	75–	1	0	0
Totals 50	45–78	47	3	6

of erythrocytes may in some way decrease the toxicity of the citrate.

To determine whether citrated whole blood would be better than citrated plasma a series of 50 dogs were bled and the blood was allowed to flow into a sodium citrate solution so that the final concentration of 0.25 per cent was obtained. This citrated blood was immediately reinjected into the same animal from which it was drawn. The mortality in this series was 50 per cent (Table VI), which is less than the 70 per cent mortality of the citrated plasma series, but not markedly so.

Comment. It would appear to be clear from these results, that when a patient has suffered a massive hemorrhage citrated plasma or citrated whole blood should be given slowly and with the idea in mind that a total dose of 1.5 grams for each 10 pounds of body weight may prove to be lethal. In fact, our results indicate that 0.11 to 0.15 grams of sodium citrate per kilogram may be fatal when given in plasma or whole blood after a massive hemorrhage. *That is, 1500 to 2500 cubic centimeters of citrated whole blood or plasma given rather rapidly to a 70 kilogram person after a massive hemorrhage may prove to be fatally toxic.*

VII. Heparinized plasma series. It was decided to verify the toxicity of sodium citrate under the conditions of the foregoing experiments by using a different and known nontoxic anticoagulant. A series of 50 animals were given pooled plasma containing heparin (liquaemin) in a concentration of 20 milligrams per liter of blood. Only 3 of the 50 dogs died as a result of this procedure (Table VII).

Comment. It is apparent from the 94 per cent survival in this series of dogs that (a) plasma is an adequate replacement fluid in the case of extensive hemorrhage, (b) that return of erythrocytes is unnecessary for survival of the animal, (c) that the mortality in the preceding two series was entirely due to the citrate, and (d) *that a temporary extensive decrease in blood volume is not in itself fatal* in most animals. This last point should be emphasized in considering the validity of the results of these experiments.

TABLE VIII.—SUMMARY OF BLOOD SUBSTITUTES

No. of dogs	Substitute	Lived	Died	Mortality per cent	Typical findings
50	None	8	42	84	None
50	0.9% NaCl	21	29	58	Dyspnea 2–4 hrs.
50	Serum	37	13	26	None
50	Special gelatine in 0.9% NaCl, pH 7.4	30	20	40	Increased sedimentation
50	Citrated plasma	15	35	70	Respiratory arrest, fibrillation
50	Autotransfusion (citrate)	25	25	50	Respiratory arrest
50	Heparinized plasma	47	3	6	None
10	Pectin	0	10	100	Respiratory depression
6	Acacia I	1	5	83	Fibrillation
11	Acacia II	1	10	91	Fibrillation
17	Acacia III	5	12	71	Fibrillation
10	"Plasmagel"	0	10	100	Fibrillation

Miscellaneous blood substitutes. Three acacia solutions from different manufacturers and one pectin preparation were tested. The mortalities were 5 out of 6, 10 out of 11, and 12 out of 17 for the three acacias. When pectin was tested on 10 dogs, all the animals died rather promptly. The findings for all substances tested are listed in Table VIII. These substances all cause pseudo-agglutination, which is sufficient to be fatal after an extensive hemorrhage.

DISCUSSION

We believe that the method devised by us for the evaluation of blood substitutes is an adequate one for their evaluation. It is drastic to the extent that if a solution is ineffective, or is in itself toxic, these effects will be manifested in the form of a high mortality. On the other hand, the animals will survive if a nontoxic and efficacious medium is given.

The prompt but temporary recovery of most animals on saline injections indicate that this procedure has value in case of emergency, with the obvious necessity of further treatment with a more potent preparation with the least possible delay. In this latter category may be placed heparinized plasma or serum. Regarding gelatin, the material we have used is definitely superior

to citrated plasma and to the other artificial blood substitutes tested, but it falls far short of perfection. Further refinement of the product is required; in this connection it is encouraging that the mortality has been brought down from 100 per cent on the first products tested to a final magnitude of 40 per cent.

The high toxicity of citrate when given in the amounts required as an anticoagulant for the large volume of plasma required under our experimental conditions is, we believe, a contraindication for the use of citrated plasma when hemorrhage is extensive. The reason for the great superiority of heparinized plasm over serum is at present obscure. It is obviously not due to the presence of fibrinogen in the one and its absence in the other, but more likely to certain alterations in the protein content which occur during the preparation. Varying degrees of serum toxicity have been reported (3, 14). Acacia and pectin, as now available, are totally unsuitable as blood substitutes when the hemorrhage is extensive.

SUMMARY AND CONCLUSIONS

1. After a massive hemorrhage, such as occurs after the section of a large peripheral artery, the intravenous infusion of normal saline solution will save some lives. The hemorrhage used in these experiments had a mortality of 84 per cent. This was reduced to 58 per cent when saline was given after the hemorrhage.

2. Pooled serum proved to be better than normal saline, the mortality from the hemorrhage being reduced from 84 to 26 per cent.

3. When citrated plasma or citrated whole blood was used, the amount of citrate that had to be given in replacing the blood lost was toxic. *Hence, caution must be exercised in giving citrated plasma and citrated whole blood in quantities of more than 1200 cubic centimeters to patients who have lost from 40 to 50 per cent of their blood. This is especially true when the citrated whole blood or plasma is given rapidly.*

4. Heparinized plasma was found to be the safest and most effective blood substitute tested, since the mortality from the hemorrhage was reduced from 84 to 6 per cent. Heparinized plasma is an adequate replacement fluid in the case of extensive hemorrhage; the return of erythrocytes is unnecessary for survival of the animal.

5. All the gelatins we have studied, with the exception of two, cause marked pseudoagglutination of erythrocytes. A gelatin which caused the least pseudoagglutination *in vitro*, reduced the mortality from the hemorrhage from 84 to 40 per cent.

It is believed that if a gelatin can be found which will cause no pseudoagglutination, it will prove to be a good blood substitute for emergency use. "Plasma gel" was not found to be suitable.

6. The gum acacia and pectin solutions we have used to date cause pseudoagglutination and have lethal effect when used as a blood substitute after a massive hemorrhage. That is, after two-thirds of the red blood cells have been lost, the pseudoagglutination of the remainder by gelatin, acacia, or pectin may be fatal.

7. It is believed (a) that the citrated human plasma now available for use should be accompanied by the precaution that it be injected slowly and not in unlimited quantities in patients who have suffered a massive hemorrhage; and (b) that the label should carry a statement regarding the toxicity of sodium citrate.

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SLIDING OR PARAPERITONEAL HERNIA OF THE PELVIC COLON

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SLIDING hernia may be defined as an extrusion of an organ in such a way that the visceral peritoneum forms part of the sac. In other words, it protrudes alongside the sac, that is, paraperitoneally (Fig. 1). It may appear to be within the sac, but it is not completely surrounded by it.

The term sliding hernia[1] has never seemed appropriate to many of us because these hernial masses cannot slide back into the abdomen without carrying the sac, in part at least, with them. The contents of an ordinary hernia may slide readily because of the slippery covering of two layers of peritoneum, both completely surrounding the extruded viscus: the visceral layer or serosa, and the hernial sac which in ordinary hernias corresponds to parietal peritoneum. In a paraperitoneal or sliding hernia, the viscus is incompletely covered by the same two layers and there is an area which is devoid of peritoneum altogether.

It is said that a sliding hernia may be suspected before operation by palpation, by the broadness of the internal ring and by the ineffectiveness of a truss. However, the diagnosis of the sliding or paraperitoneal nature of the hernia is usually made only at operation. It, therefore, behooves all who treat hernia patients to know how to manage this type safely. Recognition of the condition and understanding of its true pathological anatomy are of great importance, not only for the cure of the hernia but also for avoidance of surgical errors which may endanger the life of the patient.

"... The sac in such cases is not complete, being deficient at the posterior and outer part of the gut, where natural cellular connexions exist ... strangulation is less liable to occur. ... 'It is,' says Scarpa, 'by carrying the incision too much along the outer side of the hernial tumour that the operator fails to open the sac in this variety of hernia ... when he has arrived at the cellular covering of the intestine, would not scruple to divide it, and thus would only be made aware of his mistake by the discharge of the faecal contents.'" (3).

Moschowitz in 1925 emphasized the mistakes in the diagnosis and treatment of sliding hernias, and described the rational surgical management. Graham in 1935 gave a clear and concise account of the condition with diagrams which depicted the abnormality and its correction. Unfortunately, the facts set forth by these authors have not had the widespread acceptance they deserve.

The distinction between a paraperitoneal or sliding hernia and an ordinary hernia with adhe-

[1]English: Sliding, slip, slipped, gliding, extrasaccular, parasaccular, paraperitoneal. German: Gleitbruch, French: Hernie par glissement. Italian: Ernia per sdrucciolarmante. Latin: Hernia labens.

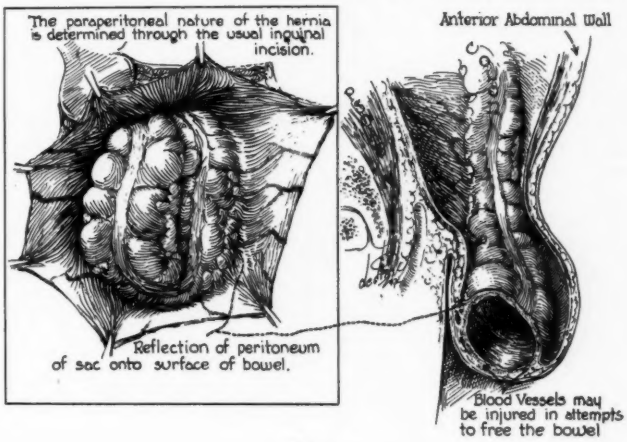
The paraperitoneal nature of the hernia is determined through the usual inguinal incision.
Anterior Abdominal Wall
Reflection of peritoneum of sac onto surface of bowel.
Blood Vessels may be injured in attempts to free the bowel

Fig. 1.

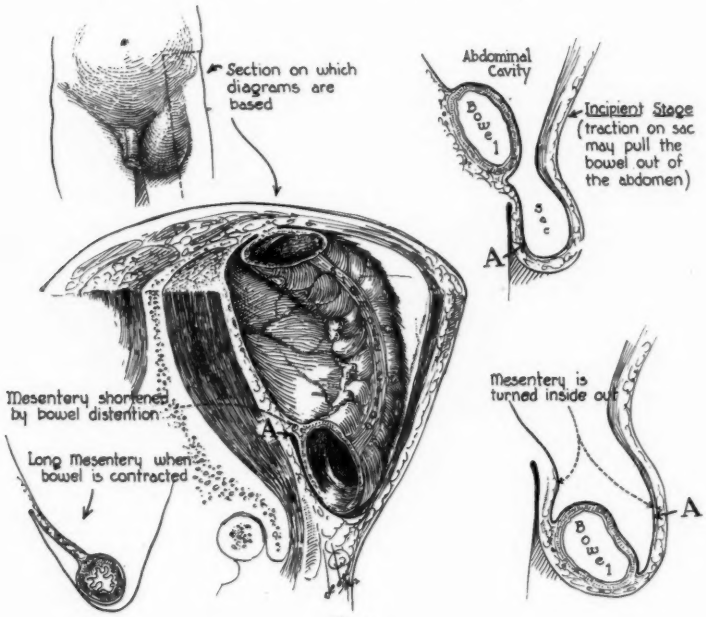

Fig. 2.

sions to the sac should be clearly understood. Adhesions may be safely cut preparatory to reduction, excision of the sac, and repair. But in a patient with sliding hernia, attempts to free the bowel may injure its blood supply.

Even when the diagnosis is understood, there are dangers to the bowel and its blood supply inherent in certain unanatomical methods of repair which have been described and which are apparently in common use. It is difficult to close the deep inguinal ring properly and safely unless the bowel is not only reduced but also kept away from the groin. Some operations designed to reconstruct the mesentery and invert the sac by successive pursestring sutures may kink the bowel or leave raw areas within the abdominal cavity and tend to fasten the bowel at the groin where it is endangered by the placement of stitches for closure of the large internal ring and the inguinal canal.

The urinary bladder may enter the inguinal canal along with a peritoneal sac as a true sliding or paraperitoneal hernia. This condition is easy to understand because the bladder is normally an extraperitoneal organ. The relationship of the peritoneal folds may be somewhat confusing when there is a paraperitoneal hernia of an organ such as the pelvic colon that is normally completely surrounded by peritoneum, both visceral and parietal. This may also happen to the terminal ileum when it descends as a sliding or paraperitoneal hernia with the cecum. The leaves of the mesentery unfold and turn inside out to form the hernia sac (Fig. 2).

In a fixed cadaver, the layers of the sigmoid mesentery are very definitely demarcated, but in life the mesentery is a variable fold. The peritoneum is not very stretchable; when the bowel distends the leaves of the mesentery separate to become serosa of the bowel (Fig. 2). The parietal peritoneum is especially movable over the underlying tissues in the lower parts of the abdominal cavity and the pelvis. The position shifts in accordance with visceral demands. This movability is familiar to us in peritonizing raw surfaces after the excision of various organs. When one remembers these physiological changes in the position of the peritoneum it is not difficult to understand how the sigmoid mesentery may be unfolded in such a manner as to place the colon in the retroperitoneal or paraperitoneal position of a sliding hernia.

METHOD OF REPAIR*

Small sliding hernias may be safely and adequately repaired by simple reconstruction of the

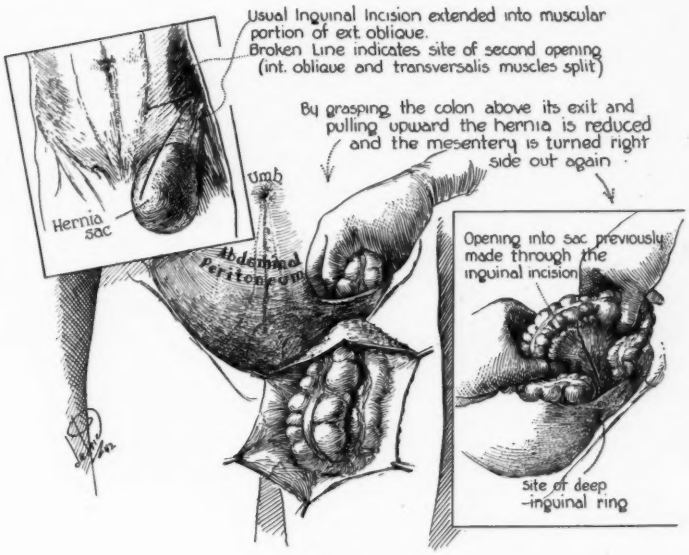
Usual Inguinal Incision extended into muscular portion of ext. oblique.
Broken Line indicates site of second opening (int. oblique and transversalis muscles split)
By grasping the colon above its exit and pulling upward the hernia is reduced and the mesentery is turned right side out again
Hernia sac
Umb
Abdominal Peritoneum
Opening into sac previously made through the inguinal incision
Site of deep inguinal ring

Fig. 3.

groin through the usual incision. But many dangers are eliminated when a separate incision into the peritoneal cavity is used to reduce the hernia and repair the peritoneum while it is held away from the groin. A low rectus incision may be used (1, 9). It is simpler to retract the upper part of the herniotomy wound, strip the external oblique aponeurosis upward, and enter the peritoneal cavity by separating the fibers of the internal oblique and transversalis muscles in the direction of their fibers (Fig. 3). This technique is essentially the same as has been described by Torek for appendectomy in combination with herniorrhaphy. LaRoque (4, 5, 6) emphasized the advantages of such an approach for operations on inguinal hernias.

We believe that the muscle splitting incision should be made some distance from the deep inguinal ring to avoid leaving a narrow band of muscle devoid of nerve supply.

Through this upper incision the bowel is grasped above its entrance into the groin and reduced by traction. This maneuver pulls the bowel out of the groin and brings with it the peritoneum which formed the sac. It is interesting to note that when the bowel is brought up the opening which has been previously made at or near the fundus of the hernia sac may now be found at the mesenteric border of the colon (Fig. 3). The sac is made up largely of the lateral leaf of the mesentery of the iliac colon, which has been turned inside out.

After reduction, the opening in the sac is closed with a running suture which is carried along to fold together any redundancy of peritoneum that is present. It may be considered a wise step to anchor some stitches through to the medial leaf of the mesentery at an avascular point near its root.

The structures of the inguinal canal are then reconstructed by whatever method seems wise. Suture of the transversalis fascia may be carried out completely because the bowel and its vessels have been removed from the site of operation. The upper incision is not closed until after the deep layers of the inguinal canal have been repaired so as to allow palpation and inspection of the repair of the groin from within the peritoneal cavity.

SUMMARY

Sliding or paraperitoneal hernias of the pelvic colon present certain difficulties and dangers when repair at the inguinal canal is attempted. A separate opening into the peritoneal cavity enables one to demonstrate that in such cases the sac is largely composed of the mesentery of the colon turned inside out. Traction on the bowel above its entrance into the hernia restores the normal anatomy of the peritoneum by turning the

everted mesentery right side out again. Appropriate repair of the inguinal canal is made simple and safe when the bowel is carried away from the groin.

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ENTERIC INTUSSUSCEPTION IN ADULTS

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TO introduce this paper, two statements are quite essential as a working basis. First, acute enteric intussusception in the adult is an entity that is encountered only occasionally during the lifetime of the average surgeon. Second, polyps in the colon are quite common, and their occurrence in the small intestine is rather rare, but a combination of polyps in both the large and small bowel is almost unique.

This statement serves to clarify the purpose of this paper. The case to be reported is one of an acute jejunal intussusception which occurred in an adult in whom we later discovered multiple polyps of both the large and small intestine. Such a case seems to warrant reporting.

CASE REPORT

E. E., a 25 year old white male, complaining of pain in the abdomen and across the lumbar region, was admitted to the Station Hospital, Fort George G. Meade, Maryland, on January 10, 1941.

The essential history dated back to 1935, at which time he suffered an attack of pain in the rectum associated with bleeding, a constant desire to defecate, and a mass which protruded from the anus. He was taken to a hospital and a polyp with a long pedicle was snared off. Following this experience, the patient was quite well for the next 4 years. In 1939 he suffered another episode almost identical to his first attack, and a polyp was found and removed. Again there was a period of partial well-being until the onset of his present illness which took place on December 21, 1940. However, the patient did recall having had a persistent backache and marked constipation during the past year.

On December 21, 1940, while on duty at Camp Livingston, Louisiana, about one hour prior to going on Christmas leave, the patient developed sudden severe pain in the lower left abdomen. He was able, however, to start a trip to his home in Wisconsin. The pain gradually subsided but was followed by a feeling of nausea which returned several times during his stay at home, and on a few occasions he actually vomited. He returned to his camp in Louisiana on January 2, 1941, still not feeling well, but he did not seek medical attention.

On January 6, 1941, he was ordered from Camp Livingston to Camp Holabird, Maryland, arriving there late the night of January 8, 1941. During the entire trip the patient ate very little and was disturbed by nausea, vomiting, abdominal cramps and backache, but constipation was no worse than usual. The following day he developed a frequency of urination, having to void about every half hour, and the pain in his back had become more severe. On January 10, 1941, he was transferred to the Station Hospital, Fort George G. Meade, Maryland, with a tentative diagnosis of perirenal abscess.

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The patient was seen by one of us (W. H. G.) on admission and found to be markedly dehydrated. There was excruciating tenderness over both kidneys. The abdomen was mildly distended with no rigidity and no local tenderness, but rather a vague diffuse discomfort on deep pressure. There had been no bowel movement for over 48 hours so an enema was given. The fecal material obtained showed no evidence of the presence of blood. Rectal examination was negative, as was a spot film of the abdomen. Urine revealed 4 plus albumin, specific gravity 1.035, with clumps of leucocytes, many granular casts, bacteria, and yeast cells seen on microscopic examination. Blood pressure was 124/80; pulse, 86; temperature, 100.6 degrees Fahrenheit. Complete blood picture was normal except for leucocytosis of 15,300.

The entire picture was most confusing and it was felt that the original impression of perirenal abscess was probably the most likely. The patient was given a large amount of intravenous fluids and tolerated a moderate intake of water by mouth without vomiting. He was observed frequently during the next 12 hours with little or no change in condition. However, about 5:00 a.m. on January 11, 1941, after having been able to rest rather well without sedation, the patient experienced extreme pain in the abdomen and vomited some dark brown fluid which contained blood. The abdomen was somewhat more distended and had a "doughy" feel to it. The pain had entirely left the renal region and centered around the umbilicus. Peristalsis was audible. Impression of acute intestinal obstruction was made and the patient prepared for operation.

Operation was performed by Dr. W. H. Gerwig, Jr., January 11, 1941. Under pontocaine spinal anesthesia, the abdomen was opened through a long right paramedian incision. A hard mass which could be delivered was located lying in the pelvis. This was found to be a gangrenous, irreducible intussusception involving about 2½ feet of the jejunum. A resection of the mass was carried out and an end-to-end anastomosis was performed. Hurried examination of the adjacent bowel revealed no palpable polyps. The abdomen was closed in layers without drainage. The specimen removed was then opened, and no organic etiological lesion such as a polyp could be found (Fig. 1).

During the next few days, the patient had a rather stormy course but began to improve gradually and was allowed up after 17 days.

One morning about 4 weeks following operation (February 16, 1941) the patient was having a stool and a small mass passed the anus but was attached higher up by a long narrow pedicle. The pedicle was ligated and cut, with great relief to the patient. He then admitted that at each stool for the past week he felt a dragging down type of pain in the lower left abdomen.

The patient was allowed several weeks convalescence after which a careful survey was begun. Repeated proctoscopic examinations were negative, and no information was obtained from 2 barium enemas (Fig. 2). Urine findings no longer showed any indication of renal damage.

It was not until a double contrast barium enema x-ray visualization was carried out that any positive information could be gained. The colon was first filled with barium which was then expelled, after which the colon was inflated

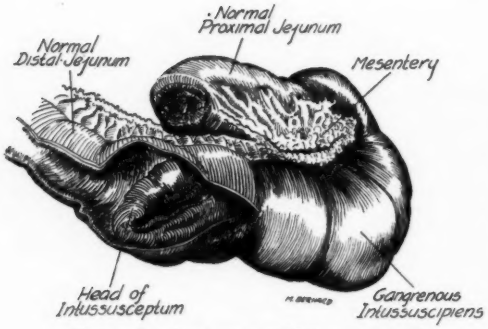

Fig. 1. Specimen removed but not opened.

with air and x-ray pictures were taken. These films clearly showed flecks of barium that had adhered to and definitely outlined several large polyps located in the region of the splenic flexure and sigmoid (Fig. 3).

On May 19, 1941, the patient was discharged on a certificate of disability after arrangements had been made for him to be sent to the Church Home and Infirmary Hospital, Baltimore, Maryland. He was admitted to that institution on May 21, 1941, and preparations for operation were begun.

Operation was performed by Dr. Harvey B. Stone, May 26, 1941. Under general anesthesia the abdomen was opened through a left paramedian incision. The site of the original anastomosis was found to be about 3 feet distal to the ligament of Treitz and was well healed and patent. A polyp, about the size of a normal adult ovary, was located some 12 inches proximal to the original anastomosis. The jejunum was opened, the pedicle ligated, cut, and the polyp removed. The jejunum was then closed. No other polyps could be felt in the small intestine. The large intestine was then explored and 5 polyps could be felt in the region of the splenic flexure and a resection of this area was carried out aseptically over Stone clamps. The abdomen was then closed in layers without drainage. The patient had a satisfactory course and was discharged June 19, 1941. Since that time the patient has written to us at 2 month intervals and states that he has been symptom free and in excellent health.

When the section of colon removed at operation was opened, not only were the 5 palpable polyps found, but numerous others too small to be felt were seen on the mucosal surface (Fig. 4). Microscopic sections of the colon and jejunal polyps revealed a characteristic type of adenomatous neoplasm. This completed the proof that ours was a case of multiple adenomatous polyp involving the small and large intestine, one of which had probably caused the acute jejunal intussusception.

It is difficult to explain the confusing symptomatology indicative of kidney disease which the patient manifested when first seen. This is especially true since the urine cleared up so rapidly. We believe that the disturbance of fluid balance caused by dehydration was too great a burden for his borderline renal capacity and that he developed a renal azotemia with urinary changes. When the fluid balance was readjusted, kidney function returned to normal.

DEFINITION, CLASSIFICATION, MECHANISM AND ETIOLOGY

Intussusception is a term used to designate a condition in which there is invagination of one part of the intestines into an adjacent part. The portion that is invaginated is called the "intussusceptum," and the portion that receives this indigitation is known as the "intussuscipiens."

From an anatomical standpoint, 4 definite varieties are recognized: (1) enteric, (2) ileocecal, (3) ileocolic, and (4) colic.

These terms merely designate the site at which the intussusception occurs. The enteric and colic types may occasionally be multiple. At autopsy, we sometimes see multiple intussusceptions which are of no clinical significance, but are merely the result of changes that take place in the bowel at the time of the patient's death.

On the basis of etiology there are 2 types, the primary and the secondary. The primary or acute type is not uncommon and occurs chiefly in infants at the ileocecal region. There is usually a sudden onset. An underlying lesion is seldom found in these cases, and when once reduced they do not usually recur. The secondary or chronic recurrent type usually occurs in adults or older children and an organic causative factor is frequently present which, if not removed, will tend to cause recurrence. Various conditions have been reported as the cause of the secondary type of intussusception and will be discussed more fully later in this paper.

The mechanics of intussusception when an organic lesion is present are more than a simple traction of the lesion. Poston reported a case of enteric intussusception in which the tumor was proximal to the invagination. In our own case no tumor was found when the affected area was resected, and it was only at the second operation that an adenomatous polyp was discovered a number of inches proximal to the previous anastomosis. By drawings and illustrations of surgical specimens, Wardill showed that the lesion which actually causes a secondary intussusception may be proximal to the invagination, in the intussusceptum, or at the apex. Therefore, he is of the opinion that the process is one of more than mere mechanical traction, and is actually assisted by spasm of the bowel at or near the site of the offending lesion. When the spasm occurs, there is relaxation of the intestine just distal to the spasm so that the contracted portion may be received. We believe that this is probably a satisfactory conclusion. However, he goes further and attempts to put the primary intussusception of infancy on the same footing as the secondary in-

Fig. 2, left. Roentgenogram after barium enema, negative.
Fig. 3. Roentgenogram showing flecks of barium adherent to and outlining polyps in region of splenic flexure.

tussusception of adults, and states that in these babies there is a definite inflammation of lymphoid tissue in the terminal ileum. When this condition is present, spasm of the bowel at this site takes place, with relaxation of the ileocecal valve and cecum. The contracted or spastic ileum is then drawn into the relaxed cecum by the longitudinal muscle fibers. However, until more substantial proof is available, this process must remain purely hypothetical. Ladd and Gross reported 372 cases of intussusception in children, 87 per cent of whom were under the age of 2 years. In 354 of these cases, pathogenesis of the intussusception could not be found.

Regardless of the cause, intussusception of the small intestine is extremely rare. McClure relates only 7 such cases in 350,000 patients admitted to the Henry Ford Hospital. Large bowel intussusceptions in adults are more frequent. MacDermott reported 5 cases of this type that occurred in his practice in less than 1 year. Webb and Sheinfeld reviewed 4 cases that they observed in a rather short period of time.

As has been previously mentioned, there are many lesions reported as the cause of the adult or secondary type. Benign and malignant neoplasms, Meckel's diverticulum, gumma, ulcers of dysentery, typhoid fever and tuberculosis, enterocysts and parasites such as round worms have all been mentioned in the literature.

It is generally agreed that neoplasms are by far the most frequent cause of secondary intussusception. However, many of these tumors may never give rise to the condition. In the large bowel the chief offender is a malignant tumor while in the small intestine benign neoplasms, especially the adenomatous polyps and lipomas, are most often encountered as etiological factors. In 1917 King was able to collect from the literature only 47 cases of benign tumors of the small gut. In 1931 Raiford reviewed the records of the Johns Hopkins Hospital and found 34 primary benign neoplasms of the small bowel, about 60 per cent of which were adenomas. Rankin and Newell in 1933 reviewed 35 cases of true primary benign tumors of the small intestine, which represented the total number at the Mayo Clinic. At that time, theirs was the largest series of its kind. They found that the benign growths occurred less frequently than

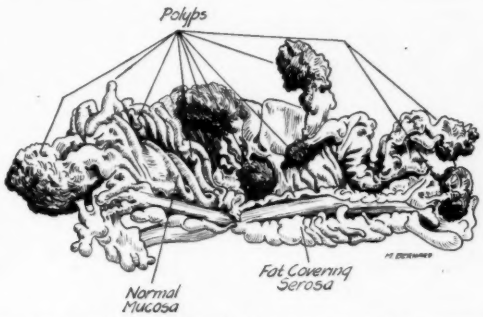

Fig. 4. When section of colon was opened numerous small polyps on mucosal surface were disclosed in addition to the 5 polyps which were palpable.

the malignant variety, but of the benign tumors, the adenomas made up the greater number of cases. Fiske also found that adenomas occur more than any other benign tumors of the small intestine but are only rarely present in the jejunum. Botsford and Newton, Cooper, and other men feel that lipomas are the most common benign tumors of the small intestine. Poston in 1935 was able to collect only 64 cases from the literature. During the same year Kirshbaum found 12 benign tumors of the small bowel in 5,754 consecutive autopsies, 6 of which were lipomas. Comfort, Aspinall, Wilmoth, and others have collected small series of cases and believe lipomas occur more frequently.

Our opinion in the matter is that because only a small percentage of these benign neoplasms of the small intestines give rise to clinical symptoms, a true evaluation is almost impossible.

Any tumor of the intestines is a potential cause of intussusception, and unless there is a definite contraindication it should be removed. This is especially true if the growth is an adenomatous polyp, for these polyps tend to undergo malignant changes. Lawrence has reported 232 autopsy findings of polyps of the gastrointestinal tract, with malignant transformation in from 6 to 7 per cent. It is in the descending colon, sigmoid, and rectum that polyps bear the closest relationship to malignancy. This relationship is least in the small intestine and transverse colon.

In every case of adult intussusception, a careful search should be made to try to discover a causative lesion as it is frequently present, not only as evidenced by our own case, but also by reports of Oughterson and Cheever, Gissane, and Faber who all describe recurring intussusceptions requiring multiple operations for relief. However, it is not difficult to understand how easily these tumors may be overlooked when the surgeon is dealing with a distended, shocked, ill patient whose bowel is obstructed. One is naturally inclined to omit a careful search of all the intestines at such a time, and instead do as little as possible. In many cases this conservative attitude is commendable; however, it must be remembered that the cause may still be there and every reasonable effort should be made to determine what the cause is. Later, when the patient's condition permits, x-ray studies or possibly a secondary exploration may be advisable.

In the opening words of this paper we stated that the occurrence of adenomatous polyps in both the large and small intestine is almost unique. Reference is made to the 232 autopsy reports of Lawrence dealing with polyps of the gastrointestinal tract. In only 4 cases of the entire series did polyps exist in both the large and small bowel.

SYMPTOMATOLOGY

The symptomatology of infantile and adult intussusception is not the same. The intussusception encountered in young babies has a rather characteristic clinical picture. In a young healthy infant who suddenly begins to have colic-like pains, passes blood from the rectum, develops an abdominal mass, and shows signs of intestinal obstruction such as vomiting, distention and constipation, a diagnosis of acute intussusception is inevitable. On the other hand, the adult who develops an intussusception may present a variety of signs and symptoms dependent on the site and severity of the lesion. A preoperative diagnosis of intestinal obstruction is usually made and the causative intussusception found at operation. If the intussusception is in the small bowel, symptoms of high obstruction are present, and if in the colon, the picture is that of a slower low obstruction. Bleeding from the rectum is encountered only occasionally and a mass may or may not be felt. Because of the tendency to chronicity of the adult type of intussusception, a history of irregular attacks of colic-like pains without obvious etiology makes recurring intussusception a possibility to be considered.

TREATMENT

The proper treatment of either the infantile or adult type is surgical intervention unless the former is promptly reduced by an enema. In the latter, a careful search for the cause must be made. Gissane operated upon a patient with intussusception of the jejunum who gave a history of severe intermittent abdominal pain for 2 years. Simple reduction was carried out at the first operation. Four weeks later the abdomen was again opened to search for the cause. A lipoma was found and two strictures were also present which were separated by healthy bowel. He produced the intussusception and found that one stricture fell at the site of the apex and the other at the junction of the ensheathing and returning layers. This is mentioned to show that these 2 areas are the most vulnerable parts of an intussusception.

When possible, reduction is the best procedure in infantile intussusception. These little patients do not tolerate large operations very well, and when the intussusception is once reduced there is seldom a recurrence. In the adult type either reduction or resection may be carried out. The latter is often necessary, and may be followed by a primary anastomosis, or by establishing an in

testinal stoma. This may be done by any of the well known methods, such as the Mikulicz-Paul method, the Rankin method, or other similar procedures.

Tumors, when found, should be removed. When these are single or if there are only a few in different regions, they can be removed separately through simple openings in the bowel. If several are localized in a section of bowel, this segment should be removed. In case there is widespread distribution as seen in diffuse polyposis of the colon, especially when there is bleeding or beginning obstruction, a one or two stage colectomy following a primary iliosigmoidostomy would seem warranted, with fulguration of any polyps present in the rectosigmoidal stump. Polyposis of the entire colon with definite malignant changes may demand preliminary ileostomy and then total colectomy and removal of the rectum, followed by deep therapy. The 2 last mentioned procedures are extensive, mutilating operations, but they seem justifiable when we consider that polyps, especially in the lower large bowel, are precancerous lesions.

SUMMARY

A rather unusual case of adult jejunal intussusception is presented. Further studies revealed that the patient also had the almost unique condition of polyposis involving both the large and small intestine. Emphasis is placed on the importance of a double contrast barium enema x-ray visualization of the colon when performing gastrointestinal studies. The definition, classification, mechanism, and etiology of intussusception are discussed. Intestinal tumors are considered, especially those of the small bowel with reference to frequency and possible malignant changes, particularly in the adenomatous polyps. The symptomatology and treatment of intussusception are brought out with special emphasis on the necessity for location and removal of the organic etiological agent which is so frequently present in the adult type of intussusception.

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FULL THICKNESS DEFECTS OF THE CHEEK INVOLVING THE ANGLE OF THE MOUTH

A Method of Repair

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THE repair of full thickness defects of the cheek is complicated by the necessity of providing a substitute for the mucous membrane and by the fact that part of the work must be carried out in an infected field. The experiences of DeGraefe, Roux, Dieffenbach, and other pioneer workers in this branch of surgery are recounted by D'Ammon and Baumgarten in their book on plastic surgery published in 1843. In most instances repair was undertaken with no antecedent experience or precept, but the results were often very good.

Gussenbauer (9, 10), in 1877, appears to have been one of the first to undertake restoration of the cheek, including mucous membrane, with a definite plan in mind. The problem was presented by a boy 7 years old whose jaws were held together by scar tissue resulting from a gangrenous stomatitis. Gussenbauer raised a quadrilateral flap the pedicle of which was placed in front of the ear and the free end at the angle of the mouth. He then cut through the entire thickness of the cheek from the mouth to the masseter muscle and brought the free end of the flap around the edge of the masseter to the inside of the mouth and sutured it to the mucous membrane. At a second operation 4 weeks later the pedicle was cut through and the whole flap with the skin surface inward was sutured in the defect. A similar second cheek flap was later put on the raw surface of the first to provide an external covering of skin.

The idea of replacing mucous membrane by skin, apparently initiated by Gussenbauer, has been utilized in a number of procedures. Israel, in 1887, described a method of repair in which he used a flap from the neck; the pedicle was placed just behind the angle of the jaw and the distal free end was turned into the cheek defect so that the skin surface replaced the missing mucous membrane. At a second operation the pedicle was cut across near its origin and the portion of flap not already utilized was folded over on the external raw surface of the distal end to provide an external skin covering. Hahn, in the same year, described a method very similar to that of Israel except that he employed a flap from the chest with a broad pedicle placed at the clavicle. Gersuny, also reporting in 1887, replaced the mucous membrane of the cheek by raising a flap from the upper neck. The pedicle was placed along the mandible and the flap was nourished by the subcutaneous tissue only. Von Hacker, 1883, raised a flap from the neck to serve as a substitute for mucous membrane and used a second flap to cover the external raw surface. Kraske, 1888, closed full thickness defects by raising a flap from the immediate vicinity of the opening and turning it into the defect. The outer raw surface was covered with a Thiersch graft. The pedicle of the flap consisted of subcutaneous tissue without the overlying skin.

Czerny, in 1889, introduced a modification of Israel's procedure by turning under the distal end of a long flap and allowing time for the opposing raw surfaces to become firmly fused before transplanting the graft. At the time of transplantation, the end of the flap had a covering of skin on both surfaces. Bardenheuer, 1891, used a forehead flap to provide mucous membrane and a cervical flap for the skin surface. Schimmelbusch, 1892, reversed this order using the skin surface of a long cervical flap for mucosa and a flap from the scalp for the external surface.

Lauenstein, 1893, made use of a long flap from the anterior chest. A bridge of skin and subcutaneous tissue was raised from the midline over the sternum, the incisions being vertical. A second hinged flap was then outlined in a transverse direction at the lower end of the vertical flap, the pedicle of the transverse flap being placed near the margin of the long vertical flap. This second flap was turned under the vertical flap to give its raw surface a covering of skin. The distal end of the long flap with skin on both surfaces could then be freed at a later time and implanted into the defect of the cheek. Esmarch, 1899, repaired a defect of the cheek involving the angle of the mouth by using two flaps, both from the face, one raised at the upper margin of the defect and the

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other at the lower. The two flaps were then brought together over the defect, completely closing it. Mucous membrane sufficient to cover the inner surface was secured by undermining the mucosa from adjacent parts.

Horsley, 1915, lined the cheek with a flap from the neck which was inserted into the mouth through an incision made between the mandible and the overlying soft parts. A suitably shaped forehead flap nourished by a pedicle of subcutaneous tissue containing the anterior temporal artery was used for the external covering. The use of a pedicle of subcutaneous tissue reduced the scarring of the face to a minimum. Esser, 1917, and Imre, 1921, practiced a method whereby large flaps were raised from the vicinity of the defect and rotated, or otherwise moved into position. Davis, 1919, employed a large pedunculated flap raised from the outer surface of the arm with its base in the middeltoid region. The distal end of the flap was folded upon itself bringing raw surfaces together and providing a covering of skin on both sides. Contracture of the flap was prevented by stretching it over a gauze covered wire frame where it was held by sutures. It was transferred to the defect 2 weeks later.

Blair, 1921, obtained a good result by suturing the free end of a long cervical flap into a defect in such a way that the skin surface replaced the missing mucosa. The external covering was secured by gradually unrolling the flap and folding it upon itself. Lexer, 1926, used a flap the pedicle of which was placed in front of the ear and contained the temporal artery. The free end was shaped something like a pistol grip and consisted partly of the skin of the forehead and partly of the hair-bearing adjacent scalp. The hairless forehead skin was turned under to form a substitute for mucous membrane.

The repair of full thickness defects of the cheek with satisfactory restoration of function and appearance is often a painstaking and difficult matter. The number of methods devised is evidence that no completely acceptable solution has been reached. If the defect involves the angle of the mouth and adjacent portions of the lips the problem is still further complicated.

Flaps raised from the areas adjacent to the defect have a good blood supply, resist infection better than tissues brought from more remote sources, and match the surrounding skin in color and texture. Their use, however, results in further scarring of the facial region, and it is often necessary to cover the area from which they have been removed with free grafts which present color contrast with the surrounding skin.

Flaps from more remote areas, such as the chest or arm usually have a relatively poor blood supply and are susceptible to ischemic necrosis or destruction by infection. To be transferred safely, remote flaps must be raised in two or more stages to permit the development of an adequate blood supply, and it is often necessary for the patient to maintain an uncomfortable position during the healing period. They also present color contrasts with the face which are permanent, exhibit a tendency toward lymphedema which may persist for months, and tend to contract into a conspicuous, unsightly mound.

The method about to be described avoids some of the objectionable features of the procedures that have just been reviewed. Its greatest use is for full thickness defects of the cheek involving the angle of the mouth with not more than one third of the adjacent lips and extending not more than half way from the angle of the mouth to the posterior margin of the ascending ramus of the mandible. It is not applicable to larger defects because of the limited amount of skin and mucosa available for repair. The operation is carried out essentially in the following manner:

An incision is begun approximately at a point overlying the junction of the zygomatic process of the temporal bone with the temporal process of the zygomatic bone. The incision is carried posteriorly and downward immediately in front of the ear and then curved in a posterior direction around the lobe of the ear to a point slightly behind the anterior border of the sternocleidomastoid muscle (Fig. 4). The incision is then carried downward and forward along the anterior border of this muscle for about two thirds of the length of the muscle. The incision goes through the skin and subcutaneous fat but not into the muscle sheaths because the branches of the facial nerve are in close relationship to the fascia overlying the muscle.

A second similar incision is then begun at a point about 2 centimeters below the inner canthus of the eye. It is carried downward and posteriorly in a direction tangential to the posterior margin of the defect. The line of incision from this point coincides with the posterior, or lateral, border of the defect and is then directed anteriorly and downward crossing the mandible about 1 centimeter lateral to the midpoint of the chin. It is carried medially to the midline and then vertically downward to the thyroid cartilage (Fig. 4). Triangles of skin and subcutaneous tissue are then removed above and below the defect, as shown in Figure 4, so that folding will not occur when the flap is subsequently moved for-

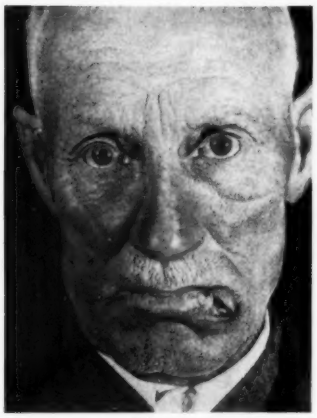

Fig. 1.

Fig. 2.

Fig. 1. Case 1. Patient as he appeared before operation. The carcinoma arising from the mucous membrane has extended through the cheek and involved the skin.

Fig. 2. Case 1. The lesion as it appeared within the mouth.

ward. The incisions just described outline what is essentially a double pedicled flap.

Elevation of this flap is begun at the posterior border and carried forward keeping always external to the fascial sheath of the masseter muscle and at a corresponding depth above and below. When the anterior border of the masseter is reached the incision is made deeper until it passes through the mucous membrane and actually enters the mouth (Fig. 5). Some of the buccal branches of the facial nerve are divided at this point but no apparent harm results. The mucous membrane is incised close to its gingival reflexion so that almost the entire remnant of mucosa will be included in the midportion of the flap (Fig. 5). Above and below level of mouth the pedicles of flap consist of skin and subcutaneous fat alone, the original level of dissection being maintained.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 3. Defect being created by removal of the cancer.

Fig. 4. Drawing illustrating defect left by removal of carcinoma and outline of double pedicled flap used to repair it. At anterior margin of flap triangles of skin and subcutaneous fat have been removed to prevent folding of skin at these points when the flap is moved forward.

Fig. 5. The flap is being elevated from a posterior approach. The dissection is carried along a plane slightly superficial to the sheaths of the underlying muscle until the anterior border of the masseter muscle is reached. At this point it extends in depth until the buccal cavity is entered.

Fig. 6.

Fig. 7.

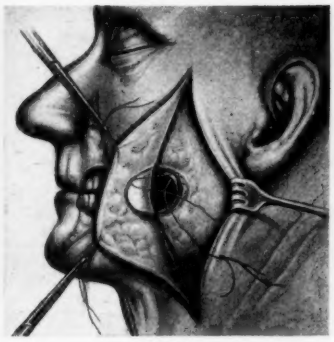

Fig. 8.

Fig. 6. The anterior margin of the flap has been raised in a manner similar to the elevation of the posterior margin. The buccal mucosa is included as a part of the flap. The dotted line indicates the position of the incision made in the underlying mucosa from the posterior approach.

Fig. 7. The entire flap has now been raised and is ready to be moved forward into the defect. The underlying mucosa is an integral part of the flap and is carried forward with it. The position of the patch of mucous membrane on the deep surface is indicated by the dotted line.

Fig. 8. A suture has been placed to illustrate the manner of resuturing the mucous membrane. The ties are made within the mouth.

The dissection of the flap is completed from the anterior approach. The pedicles above and below consist of skin and subcutaneous fat, as in the posterior part of the dissection, and mucous membrane is included in midportion (Fig. 6).

After the flap has been completely elevated (Fig. 7) sutures are placed in the posterior mucosal edges, as indicated in Figure 8, but are not tied until the anterior suture line is completed. The flap is then displaced forward to cover the entire defect. The cut edges of the lips are brought together to form a new angle of mouth, and this in turn is sutured to the anterior border of the flap at the proper level. Closure of the anterior

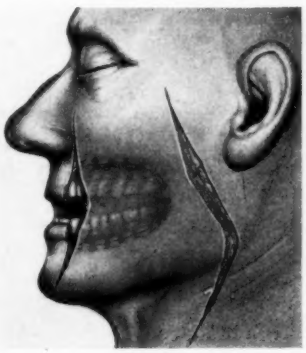

Fig. 9.

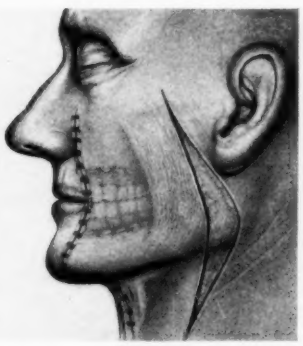

Fig. 10.

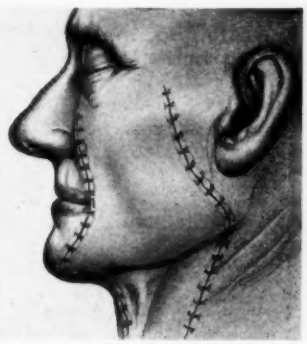

Fig. 11.

Fig. 9. In this transparent illustration the mucosa for the sake of clearness is shown completely resutured except at the anterior margin. In actual practice the posterior mucosal sutures are not tied until the anterior suture line is closed. It appears unnecessary to free completely the area of mucous membrane at its margins and then resuture it, but this step is necessary before the natural elasticity of the mucosa can be used to best advantage. The mucous membrane at posterior margin of defect can sometimes be brought together for short distance by simple interrupted sutures thereby reducing size of area to be covered.

Fig. 10. The anterior line of incision has been closed with interrupted sutures which go through all layers including the mucous membrane. In those cases in which it is found that the posterior line cannot be completely closed, the residual area may be covered with a free graft of skin.

Fig. 11. The posterior suture line is closed as the last step in the operative procedure. The depression which is present below the mandible is due to the removal of the cervical lymph nodes before the flap was sutured in place.

Fig. 12. Fig. 13. Fig. 14.

Fig. 12. Front view of patient, 5 years after operation.
Fig. 13. Lateral view, 5 years after operation. The scars are visible but not particularly conspicuous.

Fig. 14. This photograph is an illustration of the moderate asymmetry which is produced when the mouth is opened.

line is completed with interrupted sutures which include the edge of mucous membrane. The upper, lower, and posterior margins of the mucous membrane comprised in the flap are then resutured all around to the gingival mucosa from which they were cut. The suturing is conducted in part under the posterior half of the flap (Fig. 8) and partly from an anterior approach within the mouth. Usually there is sufficient elasticity to permit complete restoration. If it is necessary to leave a small defect in the mucosa it is preferable to have the deficiency at the posterior angle where healing by granulation will produce minimal interference with function.

After the closure of the anterior suture line, a defect in skin and subcutaneous tissue is left at the posterior border of the flap (Fig. 10). By virtue of the elasticity of the skin it is possible, as a rule, to close this defect completely by simple interrupted sutures (Fig. 11). In those instances in which complete closure is not possible, the defect which remains may be covered with a free graft of skin.

When the loss of tissue has been due to cancer, removal of the lymph nodes of the anterior cervical and submental triangles may be carried out 2 weeks after the reconstruction operation by reopening the lower portions of the two suture lines and re-elevating the lower pedicle of the flap. This permits a thorough removal of the nodes by dissection without running the risk of serious neck infection.

The operation described has been performed in 3 cases with satisfactory results. In each instance the loss of tissue was due to the removal of an extensive carcinoma.

Case 1. J. S., a white male, 64 years old, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Hospital February 16, 1932 for a large carcinoma of 8 months' duration involving the skin and mucous membrane of the cheek at the left angle of the mouth (Figs. 1 and 2).

On February 24, 1932, the growth was excised, the full thickness of the cheek and approximately one-third of the upper and lower lips being included. A double pedicled flap of the type here described was elevated, and a block dissection of the cervical lymph nodes of the anterior and submental triangles of the left neck was carried out. The flap was then moved forward and sutured into the defect completely closing it.

On October 19, 1932 an attempt was made to widen the mouth by making a short horizontal incision at the angle. This resulted in the development of small V-shaped defects of the upper and lower lips which had to be repaired later.

The functional and cosmetic results were considered good (Figs. 12 to 14). There was no recurrence of carcinoma. The patient died May 24, 1941 of arteriosclerotic heart disease.

Case 2. W. S., a white male, 47 years old, was admitted to St. Luke's Hospital, August 19, 1932 for carcinoma of the left cheek involving the angle of the mouth. On the following day the cancer was excised and the defect was repaired in the manner here described. The cervical nodes were removed at the same operation.

The functional and cosmetic results were satisfactory, but when the patient laughed there was a slight depression of the left angle of the mouth. This was believed to be due to the fact that at the time of operation an attempt was made to preserve the lower buccal branches of the facial nerve. This apparently resulted in a muscular imbalance,

and it appeared probable that a better result would have been obtained if these branches had been disregarded. This patient died April 17, 1933, apparently of carcinoma of the left lung. There was no local or regional recurrence.

CASE 3. E. H., a white male, 67 years old, was admitted to St. Luke's Hospital June 22, 1936, for carcinoma of the left cheek involving the angle of the mouth. The tumor was removed and the defect was repaired by means of a double pedicled flap of the type that has been described.

On July 28, 1936 the lower portions of the suture lines were reopened; the lower pedicle of the original graft was elevated and through this approach a block dissection of the lymph nodes of the submental and anterior cervical triangles was done.

The wounds healed by primary union following both operations. The cosmetic and functional results were good, and there has been no recurrence of the tumor.

ANALYSIS OF RESULTS

There were no serious complications in any of the cases, even though the primary operations in Cases 1 and 2 included cervical lymph node dissections in addition to removal of the primary tumor and repair of the defect. Better cosmetic results were obtained in the 2 cases in which no attempt was made to avoid the facial nerve fibers encountered at the anterior border of the masseter than in the one case in which a part of the fibers were spared. From the experience with Case 1 it appears inadvisable to attempt to widen the mouth by surgical means. Better results were obtained in Cases 2 and 3, and this was not done.

In cases of carcinoma, cervical node dissection can be done either at the time of repair or subsequent to it.

Advantages. From the limited experience with the type of repair that has been described certain advantages are apparent:

1. The repair is a one stage procedure, and healing by primary union may be reasonably expected. Multiple operations and a long period of hospitalization are avoided.

2. The two pedicles of the flap insure a good blood supply and greater resistance to infection.

3. The scars largely follow the natural lines of the face and within a few months become relatively inconspicuous.

4. The repair is made with skin and tissues which are a part of the face and the cosmetic result is not marred by color contrasts.

5. The general symmetry of the face is preserved when the face is at rest. Only slight distortion occurs during emotional expressions and when the mouth is opened widely.

6. No serious scar contractures occur following the operation. The upward and downward pulls tend to neutralize each other and the position of the angle of the mouth remains at the same level. The contracture in a lateral direction simply tends to widen the mouth which has been made narrow by the operation.

7. If the defect has been due to removal of cancer, a subsequent upper cervical node dissection can be done without creation of more scars.

Disadvantages. To be weighed against the advantages of the operation there are certain disadvantages which must be considered:

1. It involves some transverse narrowing of the mouth.

2. When the patient smiles or opens the mouth widely some asymmetry is apparent (Fig. 14).

3. The operation necessitates the making of additional scars on the face.

4. The method is not applicable to very large defects, and cannot be used if there has been extensive damage to the skin or mucosa adjacent to the defect. If the operation is restricted to the cases in which it is applicable, its advantages appear to outweigh its disadvantages. This conclusion is strengthened by a consideration of other methods available for the repair of such defects.

SUMMARY

A method of repairing full thickness defects of the cheek involving the angle of the mouth and adjacent portions of the lips is described.

Its advantages and disadvantages are discussed and the results in specific cases are presented.

It is applicable to moderate sized full thickness defects in the region indicated.

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CERTAIN PLASTIC PROBLEMS IN THE SURGERY OF PERIPHERAL NERVES

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IT is true of most special branches of surgery that sooner or later they interlock; and if one is on the lookout, and knows the potentialities of each branch, the sooner a suitable occasion arises. This paper deals with certain cases in which co-operation with a plastic surgeon (A.B.W.) enables a surgeon in charge of a peripheral nerve unit (J.R.L.) to simplify the problem of repairing peripheral nerves. The special features of these cases are two: (1) the absence of supple skin over the site of injury to a nerve, or (2) the situation of the wound in the skin exactly over the point of division of the nerve, so that if the steps to be described are not taken, two suture lines will be at the same level. In both cases further problems may arise because of sepsis and the deposition of scar tissue, and because of the presence, close to the nerve, of tendons which may also have been divided. The principles involved may be illustrated by a case history:

On July 26, 1941, a soldier aged 21 sustained a lacerated wound of the left elbow region, which was dealt with in hospital 5 hours after injury. Road dirt had been ground into the medial epicondyle, and there was extensive laceration of the skin and of the muscles of flexor-pronator group, with complete severance of the ulnar nerve. The wound was cleansed and excised, and the ends of the ulnar nerve were united with a stay suture and covered so far as possible with muscle. The torn skin was sutured over the cut nerve, but left open over the rest of the wound. The patient was admitted to a peripheral nerve unit on October 31, 1941, when the wound was still not healed. It presented an irregular puckered scar of roughly horseshoe shape (Fig. 1). Flexion at the elbow was limited to from 60 to 100 degrees. Pronation and supination were full.

Neurological examination. Flexor carpi ulnaris was acting, as was flexor digitorum profundus to the 4th digit; all the remaining muscles innervated by the ulnar nerve were paralyzed. Sensory loss was present over the area supplied by the medial cutaneous nerve of the forearm and the ulnar nerve (Fig. 2). Loss of postural sensation was limited to the 5th digit. There was no radiological evidence of injury to bone.

It was obvious that secondary suture of the nerve was necessary and that this would involve shortening its course by transplantation. However, the presence of unhealthy skin adherent to the medial epicondyle made this impossible. In addition, it was known that there had been considerable loss of muscle, involving that part of the origin of the flexor-pronator group in which it is customary to bury

Fig. 1. The scar of the injury just before complete healing. Flexor carpi ulnaris is seen to be contracting.

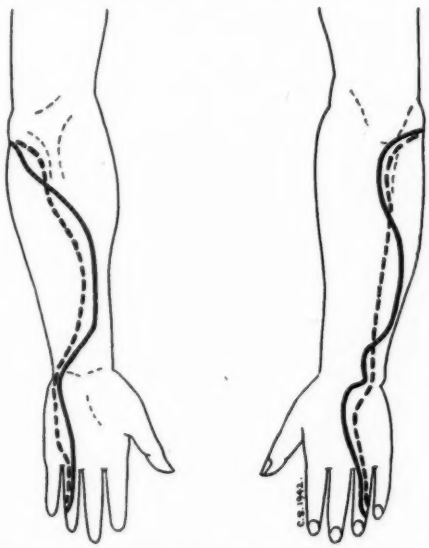

Fig. 2. Area of anesthesia, November 5, 1941. Continuous line, loss to cotton wool; dotted line, loss to pinprick.

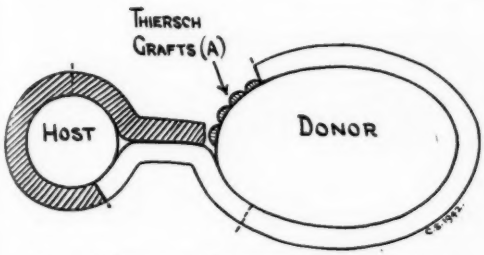

Fig. 3. Diagram of first stage of plastic operation.

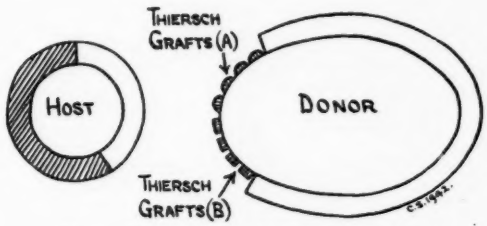

Fig. 5. Diagram of final grafting operation.

the transplanted nerve. It was decided to arrange first for the replacement of the unsuitable skin, and in the meantime to develop a technique for burying the transplanted nerve more deeply in the limb. Accordingly the patient was transferred to a plastic unit.

From a plastic point of view, the diagnosis was loss of skin and subcutaneous fat on the medial aspect of the left elbow, over an area measuring 10 centimeters by 7.5 centimeters. A pattern of this area was cut in jaconet, and from this a suitable donor area was mapped out on the adjacent thorax and abdomen. At the first operation (A.B.W.) the area of scar on the arm was dissected from its medial boundary to the median line of the scar, and raised as a flap. The anterior half of the donor area was raised as a flap of skin and subcutaneous tissue, hinged posteriorly, and turned so that its (previous) anterior margin could be stitched to the medial margin of the defect in the arm. The remainder of the donor flap received the flap raised from the arm. The raw area of the donor site was covered by a Thiersch graft (Fig. 3). Three weeks later a delaying operation was carried out (A.B.W.) to encourage vascularization from the humeral attachment of the donor flap; under local anesthesia, the donor flap was mapped out from the pattern, raised from the deep fascia except for two small areas at the posterior angles, and stitched back into its previous position (Fig. 4). Ten days later, under general anesthesia, the excision of the scar tissue in the arm was completed (A.B.W.) the donor flap completely detached from its original situation and stitched into its new position, and the remaining raw area of the donor site covered by a Thiersch graft (Fig. 5). All stitches were removed on the 7th day. The graft took well, except for a small area at its distal and medial edge, where epithelization was completed by a few pinch grafts (Fig. 6).

The patient returned to the peripheral nerve unit for secondary suture of the ulnar nerve[1] on March 22, 1942, after a period of massage to the graft. On this date the neurological examination showed certain differences from that carried out on admission. Postural sensibility had been recovered in the 5th digit, except at the terminal joint, although the part of flexor digitorum profundus acting on the 4th and 5th digits was not now active. The patient felt and localized a pinch on the analgesic border of the hypothenar eminence, and it was of great interest that the upper portion of the skin graft had recovered some sensation (Fig. 7).

At operation on March 26, 1942 (J.R.L.) the incision (Fig. 8) exposed the ulnar nerve in the arm and then joined the edge of the skin graft so as to leave no acute angle, followed the medial edge of the graft to its distal end, and then diverged along the course of the ulnar nerve; the small area at the lower end of the graft, which had been completed by pinch grafts, was excised. The graft was then turned laterally over the elbow joint and found to be well vascularized and bleeding freely. The ulnar nerve was

[1]Learmonth, J. R. "A Technique for Transplanting the Ulnar Nerve." Surg. Gyn. Obst., 1942, 75: 792.

Fig. 4. Appearance after delaying plastic operation. The flap is connected to the donor area at its posterior corners only.

Fig. 6. The graft in position, and healed.

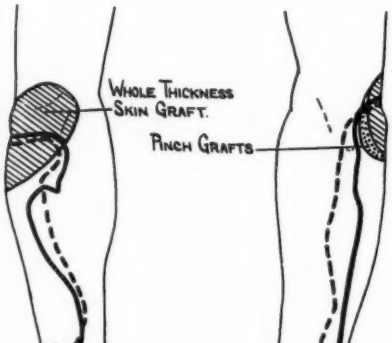

Fig. 7. Area of anesthesia, March 22, 1942. Note that sensation has returned over the proximal part of the graft. Continuous line, loss to cotton wool; dotted line, loss to pin-prick.

freed from its groove to a distance of 1 centimeter below the epicondyle, and in doing so a branch to the elbow joint and one branch to flexor carpi ulnaris were sacrificed. Below this level the nerve was involved in dense scar tissue as it passed between the two heads of flexor carpi ulnaris. The dissection was therefore transferred to the distal part of the incision, and carried proximally until scar tissue was again reached. The neuroma was 6 centimeters long and had a maximum diameter of 1.8 centimeters. It was extremely hard in consistence and had united firmly to scraps of muscle in the neighborhood. A tunnel was now made by passing a hemostat under the flexor pronator origin; the nerve was divided distal to the neuroma and drawn through the tunnel from above downward. As it was clear that the suture line would lie under the muscles, and as their superficial layers were extensively scarred, it was thought best to resort to the technique which had been elaborated, and to detach the flexor-pronator group from the medial epicondyle. The ulnar nerve could then be placed beside the median nerve in the depths of the wound, in an intermuscular plane providing the most favorable conditions for suture; so impressive were the advantages of this procedure that it has been adopted as the routine

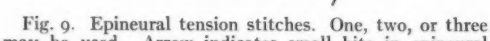

Fig. 9. Epineural tension stitches. One, two, or three may be used. Arrow indicates small bite in epineural sheath.

Fig. 8. Arm after secondary nerve suture. Note placement of incision to avoid acute angles with the edge of the graft, and healing without any loss of graft.

operation for tardy ulnar palsy in all subsequent cases. Suture of the nerve was carried out with fine black silk, with 2 epineural tension stitches used in the unit as splint stitches when long gaps have to be overcome (Fig. 9). The flexor-pronator group of muscles was then sutured back into position with interrupted catgut sutures, and the flexor carpi ulnaris trimmed and repaired as completely as possible. The wound in the skin came together without tension, and although the graft area looked a little pale, there was really no concern about its vitality. The arm was put up in a light plaster with the elbow in 60 degrees' flexion and the forearm pronated. On return to the ward, the patient was given a dose of 3,000 units of antitetanic serum and a course of sulfathiazole was started. The arm was left undisturbed until April 15, 1942, when the plaster was removed; the wound was found to have healed by primary union without any loss of graft (Fig. 8). The posterior half of the splint was reapplied, and worn for 6 weeks after the operation.

At this time, when the patient was discharged, the skin including the graft, was quite healthy and mobile. Extension and flexion at the elbow joint were still restricted, no doubt from primary loss of muscle tissue, but pronation and supination were almost normal. The area of sensory loss remained the same, there being no further recovery of sensation in the graft. An interesting finding was the presence of goose-skin on stimulation by cold in the lower part of the skin graft, in an area in which sensory recovery had not yet begun.

In this case the plastic procedure converted a difficult problem into a simple one. Lacerated wounds about the elbow region are not uncommon, and it is hoped that the plan we adopted will commend itself to other surgeons who encounter similar cases.

The wound which divides nerves and possibly tendons at the same level as the skin is seen most often on the anterior aspect of the wrist. In war time it is not often possible to perform primary suture of tendons and nerves, and in many cases the wound has been infected. Thus when deliberate surgery becomes possible, the patient is found to have a thin puckered scar, lacking even the modest layer of subcutaneous tissue which facili-

tates movement at the wrist. To this scar the ends of severed tendons and nerves are often adherent; even if suture has been attempted, these adhesions may form. Their presence reduces the range of movement in repaired tendons, and as the line of suture of the nerve(s) is immediately below the line of skin suture, the two may adhere, the result being a locally tender scar, which is often painful during movements of the fingers, and which may give rise to paraesthesia in the territory of the severed nerve, varying in intensity from the occasional and merely annoying type to the continuous and crippling type. Moreover, it is notoriously difficult to excise these scars, because there is little spare skin in the region; and those who deal with such cases know that it is a mistake to attempt to secure union without tension by hyperflexing the wrist. In such cases we advise that a quadrilateral area of skin including the scarred area be excised by sharp dissection, so as completely to free the underlying nerves and tendons. The extent of this area is shown in Figure 10. Distally the line of excision follows the proximal crease of the wrist, proximally it crosses the forearm transversely at least 5 centimeters above this crease, and laterally it follows the borders of the forearm. The method of attaching the graft follows that already described for the elbow. Movements of the fingers may be continued while the flap is changing its source of nourishment. When its vitality is assured, repair of the nerves (and tendons) is carried out through an incision which follows the crease round the base of the thenar eminence for 3 to 4 centimeters before joining the edge of the graft at a right angle. Thereafter it follows the edge of the graft to radial or ulnar side according to the nerve involved; when both nerves must be sutured, the exposure is best when the incision passes to the ulnar side. An additional incision runs proximally toward the medial part of the antecubital fossa, from the junction of the medial and middle thirds of the proximal border of the graft. The graft is raised by sharp dissection to one or other side, and the vertical incisions are undercut if necessary. Through this exposure the nerve trunks can be freed upward and downward as far as is necessary and possible, and the continuity of nerves and tendons can be restored by suture lines which lie under normal skin and subcutaneous tissue, remote from any cutaneous scar. Finally, the incision in the skin can be closed easily without tension.

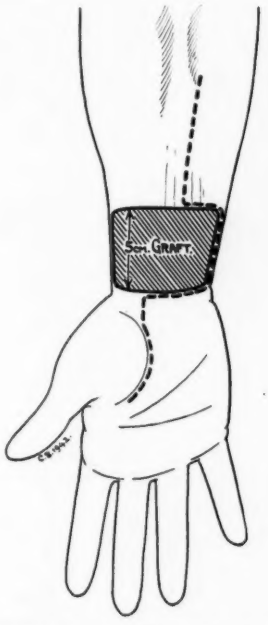

Fig. 10. Diagram to show the area replaced by a full thickness skin flap (continuous line), and the subsequent incisions for suture of nerves and tendons (dotted line).

SUMMARY

Methods are described for use about the elbow and wrist joints, when it is desired to replace skin, or so to repair nerves and tendons that the lines of suture of the latter do not lie at the same level as the cutaneous suture line.

We are indebted to Dr. A. Davidson, chief medical officer to the Department of Health for Scotland, for permission to publish this work from two hospitals in the Emergency Medical Service.

GASTROILEOSTOMY AND GASTROILEAL ULCER

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THERE are several complications which may follow gastroenterostomy. When a patient who has had a previous gastric operation presents himself with symptoms referable to the gastrointestinal tract, it is well to analyze the complaints carefully with all the possibilities in mind. The syndromes representing gastrojejunitis, gastrojejunal ulcer, malfunctioning gastroenteric stoma, and postoperative gastritis are rather common after gastroenterostomy. More infrequently, recurrent ulceration has led to formation of a gastrojejunocolic fistula, usually after an interval of time has elapsed after operation. A complication which may not be thought of, and to which we again wish to call attention, is the presence of a gastroenteric stoma which is actually gastroileal instead of gastrojejunal. This low anastomosis is the result of a surgical error.

We have found in the literature (1-7) 16 previously reported instances of gastroileostomy, including the 9 cases of Rivers and Wilbur. It is impossible to determine the general incidence of this surgical error because not all such cases may be reported. At the Mayo Clinic approximately one diagnosis of this condition is made in each 1 to 2 years.

In the present paper we wish to present 8 additional cases of gastroileostomy and also 1 case in which the patient had been seen previously at the clinic and which was reported by Rivers and Wilbur but not proved surgically until recently. All the operations had been performed prior to the registration of the patients at the clinic and in each instance subsequent confirmatory operation was performed at the clinic.

REPORT OF CASES

CASE 1. In September, 1927, a 35 year old Jewess came to the clinic complaining of abdominal pain. In 1911 she had begun to notice daily ulcer-like pain. Four days after gastroenterostomy had been performed in 1916, supposedly for a duodenal ulcer, diarrhea began, with 10 to 12 stools daily. After 2 years the frequency of the stools decreased to 4 or 5 daily, persisting this way until her registration at the clinic. Frequently, identifiable undigested food passed from the bowels within a few hours after ingestion. Vomiting occurred at times and gave relief from an epigastric hunger pain. When seen 11 years after operation the patient had lost 22 pounds (10.0 kgm.), dropping from 125 pounds (56.7 kgm.) to 103 pounds (46.7 kgm.). Her height was 61½ inches (156 cm.). No free acidity was obtained on aspiration of gastric contents after an Ewald meal. Roentgenological examination showed an anastomosis between the stomach and the lower part of the ileum, allowing the barium to pass immediately into the large bowel. There was a deformity of the duodenal cap. A diagnosis of gastroileostomy was made and surgical treatment was advised. The patient decided not to have operation then.

In July, 1941, this patient returned to the clinic with somewhat the same complaints. She had not had any surgical treatment for her low anastomosis during the interval. From 1927 to 1930 she had continued to vomit every few days and to have lienteric stools and belching with fecal odor. Her condition improved between 1936 and 1939, and she gained weight slowly. During the 2 years prior to her last visit to the clinic weakness, loss of weight, and abdominal cramps with each bowel movement developed. In March, 1941, vomiting suddenly increased and cramping above the navel appeared. This distress extended to the chest and shoulders. The gall bladder was not visualized in two cholecystograms elsewhere, and cholecystectomy had been advised. Her weight, which had averaged 118 pounds with clothing had decreased in the 4 months before admission to 95 pounds without clothing.

Examination showed only a slight loss of weight, and signs of nutritional deficiencies were remarkable by their absence. Fractional analysis of gastric contents after a test meal showed a maximal total acidity of 16, with no free acidity. The total concentration of serum protein measured 5.8 grams per 100 cubic centimeters of blood, with an albumin-globulin ratio of 2.33 to 1.0. Cholecystography failed to reveal a shadow of the gall bladder but this was attributed to poor absorption of dye resulting from the low anastomosis. Re-examination of the stomach and colon reconfirmed the presence of a gastroileal stoma (Fig. 1). The symptoms were of sufficient magnitude to indicate again the need for surgical intervention.

At operation on August 6, 1941, there was no evidence of previous ulceration of the stomach or duodenum. Neither ileitis nor gastroileal ulceration was present in the anastomosis, which was located 6 inches (15 cm.) from the ileocecal valve. The stoma was about 2½ inches (6 cm.) in diameter. After disconnection of the anastomosis the openings in the stomach and ileum were closed. The patient had an uneventful convalescence. Subsequent fractional analysis of gastric contents after a test meal revealed a maximal total acidity of 12 and no free acidity.

Even though the anastomosis only 6 inches (15 cm.) from the ileocecal valve had been present for 30 years there was no remarkable nutritional deficiency. This was undoubtedly due to good function of the pylorus. Even vomiting and lienteric stools had not harmed the patient much. This was Case 8 in the series of Rivers and Wilbur, the only one of that series in which operation was not done at the time.

CASE 2. A 35 year old woman came to the clinic in July, 1912, complaining of gas, bloating, diarrhea, weakness, and loss of weight. From the age of 18 years she had been subject to sick headaches. In January, 1912, after 18 months of indigestion which was associated with the headaches, an operation for exploration of her gall bladder and stomach

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had been performed. The appendix had been removed and a gastroenteric stoma had been established. Immediately after operation diarrhea with frequent bulky and greasy stools had developed. Gas and borborygmus bothered her much. At times she saw undigested food in her stools. There had been a loss of 25 pounds (11.3 kgm.) in the period following operation.

Examination revealed marked loss of weight. The abdomen was distended, and peristalsis was visible in somewhat distended loops of bowel. A test meal showed a total acidity of 4 and no free hydrochloric acid. There was a great excess of neutral fat in the stools. Test of pancreatic secretion showed digestion of casein and starch to be deficient. No roentgenological examination was made.

At operation it was found that the gastroenteric stoma had been made more than halfway down the small intestine, a loop of the upper part of the ileum having been used. The pancreas was thickened and covered with dilated vessels. The gall bladder was large and could not be emptied. After the gastroileal stoma had been disconnected, cholecystostomy was performed. Recovery was uneventful.

In a letter written in February, 1913, the patient stated that she had gained 1 pound (0.5 kgm.) a day for 40 days after the operation. She had not been relieved of moderate difficulties with sour stomach.

There was fairly good evidence that chronic pancreatitis with deficient pancreatic secretion played a part in the production of the patient's loose stools. The short circuit of stomach to the upper part of the ileum undoubtedly accounted for most of the symptoms, since her diarrhea disappeared and gain of weight was prompt after operation.

CASE 3. In January, 1922, a 53 year old woman complained of diarrhea and weight loss. From 1906 she had had distress of ulcer type and in August, 1916, roentgenological examination here had demonstrated a duodenal ulcer. A test meal at that time showed total acidity of 36 and free hydrochloric acid of 28. Because of progression of symptoms gastroenterostomy had been performed in March, 1921. Pain was relieved by operation, but as soon as she began to eat solid food diarrhea with 5 to 20 movements a day appeared. The stools often had a lienteric character and prunes could be seen in the stool within 3 hours after their ingestion. Periods of diarrhea lasting about 4 days alternated with periods of fairly normal stools lasting about 6 days. Once after operation she had vomited feces-like material and twice had had eructation of the same material. Her abdomen became sore during bouts of diarrhea. She had lost 36 pounds (16.3 kgm.) in the 9 months after operation.

Physical examination showed only loss of weight and slight tenderness in the lower part of the abdomen. Analysis of gastric contents by the fractional method showed anacidity until 8 units of free hydrochloric acid appeared after 1¾ hours; 95 cubic centimeters was recovered. Hemoglobin measured 74 per cent (11.2 gm.) per 100 cubic centimeters. Roentgenological examination showed a gastroenteric stoma with communication of small bowel with right half of colon. The duodenal cap was deformed.

At operation the stomach was found to be anastomosed to the ileum only 4 inches (10 cm.) from the ileocecal valve. A chronic ulcer had caused extensive contraction of the duodenum. Accordingly, after disconnection of the gastroileal stoma and closure of the openings, gastrojejunostomy was performed. Two weeks later because of symptoms suggesting obstruction, re-exploration was performed. Aside from a mild kinking of the bowel at one point nothing of great significance was found. The patient made a good recovery.

In a letter written in November, 1934, the patient stated that she had had no more illness since her operation.

CASE 4. A 37 year old marble worker in August, 1930, complained of swelling of his legs and ankles and of stomach trouble. About 1917 periodic bouts of pain had led to roentgenological examination which had indicated the presence of a duodenal ulcer. In 1927 gastroenterostomy, appendectomy, and cholecystectomy had been performed. After the operation there was no more pain but 8 months later intermittent nocturnal attacks of vomiting developed, coming approximately every 3 weeks and lasting about 1 week at a time. Three to 4 quarts (3 to 4 liters) of greenish material, sometimes containing retained undigested food, would be brought up with good relief of nausea. No diarrhea or fecal belching had occurred. Constipation required a nightly laxative. The patient had lost about 6 pounds (2.7 kgm.) in the 4 weeks before admission. About 1 year after operation weakness and stiffness of the legs had developed with associated numbness and tingling up to the knees. Similar numbness was present in the fingers. Sensitivity of the muscles of the arms and legs later led to the use of crutches. Dependent edema was present daily but disappeared at night.

Examination showed loss of weight, dependent edema, and multiple peripheral neuritis. Analysis of gastric contents disclosed a total acidity of 76 units with free hydrochloric acid of 58; 245 cubic centimeters was aspirated. Roentgenological studies showed a low, malfunctioning gastroenteric stoma with retention. There was a secondary type of anemia. A bromsulfalein test of liver function did not show any retention of dye. Serum protein measured 6.5 grams per 100 cubic centimeters of blood.

At operation the anastomosis was found to be between the stomach and a loop of the upper part of the ileum. Because of scarring and contraction below the pylorus, reconstruction of the pyloric outlet was performed after disconnection of the gastroileal stoma. There was no gastroileal ulceration, but the proximal part of the intestine was much distended and the walls were thickened.

The patient stated in a letter in 1934 that he had not been relieved completely by operation and had had some recurrence of pain, perhaps of ulcer type. It is probable that the multiple neuritis in this case was the result of vitamin deficiencies created by vomiting.

CASE 5. A 56 year old railroad section foreman in January, 1936, complained of stomach trouble and external drainage of bile. After an onset of symptoms at the age of 36 (1916) he had had distress of ulcer type mingled with gall-stone colics. In 1928, after pyloric obstruction, the gall bladder had been drained and many stones had been removed. Gastroenterostomy had been performed because of an obstruction produced by a duodenal ulcer. Operation relieved him and he gained weight for 6 to 8 months. Recurrent symptoms at that time consisted of burning crampy pain which was referred to the lower part of the abdomen or was generalized. For 7 years the patient had endured this pain, with only partial relief by milk or alkali. In 1935 he found that 2 to 5 hours after meals there would be fullness, then gas, burning, cramps, nausea, and bitter vomiting. At reoperation in July, 1935, narrowing of the gastroenteric stoma had been found. For reasons unknown to us the gall bladder had been drained and a "lump" removed from the stomach. Bile persistently drained externally after this operation, and there was a progressive loss of strength together with a loss of 36 pounds (16.3 kgm.) before his admission to the clinic.

At the time of the patient's registration at the clinic, the chief complaints were of cramping, burning pain referred to the lower part of the abdomen, vomiting, marked loss of strength and weight since his second operation, and external drainage of bile together with acholic stools and dark urine.

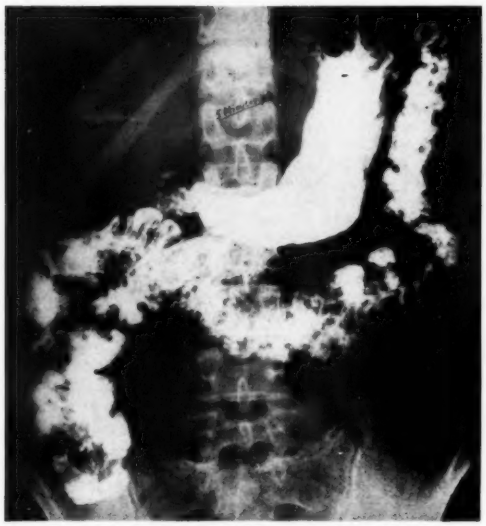

Fig. 1. Gastroileal stoma.

The patient's condition was poor. He was emaciated and dehydrated and had severe abdominal pain. Bile was draining from an external biliary fistula. On roentgenoscopic examination of the stomach a gastrojejunal ulcer with diffuse jejunitis was felt to be present, together with a deformity of the duodenal cap and some dilatation of the stomach. An Ewald test meal showed a total acidity of 60 units and free hydrochloric acid was 50; 100 cubic centimeters was recovered.

At operation there were found an anterior gastroileal stoma with a gastroileal ulcer, a healed duodenal ulcer, which had practically occluded the duodenum, and a biliary fistula which communicated with a functionless gall bladder. The gastroileal ulcer situated on the posterior wall had a crater about 1.5 centimeters in diameter and both afferent and efferent loops of ileum had contracted as a result of fibrosis. The gall bladder, which did not contain any stones, was removed. The common bile duct was normal. The gastroileal anastomosis was disconnected and the gastroileal ulcer was excised. A large gastroduodenal stoma was made, and a temporary jejunal stoma for feeding purposes established. The patient made a good recovery.

Case 6. In March, 1937, a 61 year old retired funeral director complained of vomiting. In 1928 he had first noticed epigastric distress of ulcer type. Hematemesis and tarry stools occurred in 1929, and in 1930 a milder episode of bleeding recurred. Thereafter, on a medical regimen he got along well until 1936 when nausea and retention type vomiting were shown by roentgenological examination to be due to pyloric obstruction. Gastroenterostomy had been performed in January, 1937.

Immediately after operation diarrhea had begun, with 6 to 10 stools daily for about 6 weeks. No undigested food was seen in the stools. The use of bismuth seemed to check the diarrhea but nausea, gagging, and vomiting or regurgitation followed its use. Pain or soreness was present just above the navel in periods varying from several minutes to hours. There was no definite relation of pain to intake of food but relief would follow passage of flatus. The patient had lost 60 pounds (27.2 kgm.) in the 3 months after operation.

Examination here showed loss of weight, dehydration and a slight epigastric tenderness. Analysis of gastric contents showed a total acidity of 40 units and free hydrochloric acid of 30; 50 cubic centimeters was aspirated. Chemical examination of the blood did not disclose any abnormality. There was no anemia. Roentgenographic studies of the stomach showed a gastroileal stoma with extensive gastroileitis, especially evident at the anastomosis. The gastroenteric stoma had been made with a segment of ileum 12 inches (30 cm.) from the ileocecal valve.

At operation it was found that the gastroileal stoma contained a gastroileal ulcer 1.0 by 1.0 centimeter. A subacute perforating duodenal ulcer with a mass over the head of the pancreas had shut off the duodenum almost completely. Because partial gastrectomy did not seem safe, disconnection of the anastomosis was performed with excision of the gastroileal ulcer and establishment of an anterior gastrojejunal stoma after closure of the opening in the ileum. Recovery after operation was uneventful. An Ewald test meal 24 days after operation showed a total acidity of 32 units and free hydrochloric acid of 24; 250 cubic centimeters was recovered.

Seven months after operation the patient stated in a letter that he had regained about 22 pounds (10.0 kgm.) and had good strength, a good appetite and no pain.

Case 7. A 53 year old man in June, 1938, gave as his chief complaint intermittent pain and gaseous distention below the navel, present for 23 years. Prior to 1915 he had had gnawing abdominal distress. Immediately after gastroenterostomy in 1915 he apparently had been quite ill and had had loose stools containing undigested food which had been ingested as little as 15 minutes before. Subsequently symptoms had occurred in bouts of 4 to 6 weeks' duration, with free intervals of 2 to 12 weeks, continuing throughout the 23 years before the patient's registration at the clinic. When he woke, his abdomen was usually comfortable but after breakfast, distention and a localized gnawing crampy pain at or just below the navel would appear, usually about 10 a.m. Ingestion of alkalis and food would not relieve this distress. Passage of unusually large amounts of flatus, with or without a loose stool containing undigested food, would give almost complete relief for 1 hour. The cycle recurred at hourly intervals 8 or 10 times daily, and frequently would wake the patient. Nausea might be present but vomiting did not occur. Fecal regurgitation or fecal taste had never been noticed. Weight would be lost during a spell but regained during the free interval. The patient had lost 7 pounds (3.2 kgm.) in the 3 months just before his visit to the clinic.

Physical examination showed moderate hypertension. Observations suggestive of gastroileostomy at the time of roentgenoscopic examination of the colon were confirmed on roentgenographic examination of the stomach, showing an anastomosis between the stomach and the ileum apparently about 2 feet (61 cm.) above the ileocecal valve. The duodenum did not seem abnormal. Analysis of gastric contents was not performed.

At operation the anastomosis was found to be about 12 inches (30 cm.) above the ileocecal valve. It was large enough to admit the tips of two fingers. No ileal ulcer or ileitis could be demonstrated. No evidence of duodenal ulcer was demonstrated. The gastroileal anastomosis was disconnected and the openings in the stomach and ileum were closed. Recovery was uneventful.

Approximately 1 year after operation examination showed the patient to be in excellent condition aside from hypertension. His only complaint was an epigastric burn-

ing when he was tired or nervous. Aspiration of the contents of the fasting stomach showed a total acidity of 8 units and no free hydrochloric acid. Roentgenoscopic examination showed an ulcer type of duodenal deformity.

That this patient was able to tolerate a gastroileal stoma only 12 inches (30 cm.) from his cecum for 23 years was undoubtedly due to the fact that his duodenum was normal. This of course permitted enough absorption of food in the upper part of the small bowel to prevent significant loss of weight.

CASE 8. A 34 year old salesman on July 24, 1939, complained chiefly of abdominal pain. In 1923 he had started having episodes of ulcer-like distress. In 1924 after heavy exertion an acute perforation of a duodenal ulcer had occurred and required surgical closure. After 9 months' convalescence the patient was relatively free of pain for 6 years except for short bouts of mild ulcer type once or twice a year. After a recurrence of pain in 1930 he had ulcer pain each year until 1937, at which time posterior extension of pain, nocturnal pain, a few days of tarry stools and one attack of vomiting occurred. Gastroenterostomy in May, 1937, had provided complete relief of symptoms until their recurrence in November, 1937, when there were 3 essential differences: (1) There had been a shift of the pain from the epigastric to the umbilical region; (2) extension of pain also had shifted posteriorly to the low lumbar region; (3) pain was accompanied by a distressed full feeling, relieved by one or two enemas daily. Night pain tended to occur earlier. Periodicity and modes of relief were unchanged. There had been a loss of weight of only 5 pounds (2.3 kgm.).

Tenderness was present just above the umbilicus. Analysis of gastric contents showed a total acidity of 84 units and free hydrochloric acid of 74; 150 cubic centimeters were recovered. Roentgenological study showed a duodenal deformity with some obstruction but the pylorus was patent. The gastroenteric stoma was small and, although the anastomosis was free, what was thought to be jejunitis was demonstrated.

At operation there was constriction of the old region of duodenal ulcer, with induration into the head of the pancreas and some obstruction. The gastroileal anastomosis was at a point in the small bowel at least 8 feet (243 cm.) distal to the ligament of Treitz. When this was disconnected a small ileal ulcer was found at the base of the mesentery just opposite a contracted stoma. The ulcer was excised and the ileal opening closed. Partial gastrectomy of the Pólya type was performed with removal of about half of the stomach. Recovery was uneventful.

A letter from the patient approximately 2 years after operation revealed that he was in good condition, did not have any distress and had increased his weight by 6 pounds.

The shift of pain to a lower point in the abdomen and the relief by enemas were characteristic of ileal ulceration.

CASE 9. A 58 year old farmer in June, 1941, complained of diarrhea. In 1913 he had had an isolated period of what was probably ulcer distress. During 5 months of 1932 symptoms recurred, this time diagnosed as due to ulcer. From 1935 to 1939 about 5 brief bouts of ulcer pain occurred. In February, 1939, acute perforation of a duodenal ulcer had required surgical closure, which had relieved his symptoms until May 20, 1940, when acute perforation again had required surgical closure. As a prophylactic procedure partial gastrectomy had been performed on December 27, 1940. The patient was able to go home in January, 1941, but after 1 month he lost his appetite and diarrhea developed with 6 to 12 loose to watery stools daily. These were scattered throughout the day, but he always had a bowel movement as soon as he ate. Occasionally undigested food could be seen in the stools. He was repelled by the sight of food and had lost 60 pounds (27.2 kgm.) between operation and time of his admission to clinic.

Physical examination showed moderate emaciation, dry skin and slight edema of the ankles. Analysis of gastric contents showed a total acidity of 16 units but no free hydrochloric acid; there was a fetid odor of bile to the 110 cubic centimeters recovered. Total serum protein measured 5.6 grams per 100 cubic centimeters of blood with an albumin-globulin ratio of 1:1. Several specimens of stool showed fat, undigested food and meat fibers in excess of normal. Roentgenological studies showed a posterior Pólya type of resection, the anastomosis apparently made with a loop of ileum. Barium had passed into the transverse colon and splenic flexure 1½ hours after the stomach examination.

Surgical exploration showed that at the last operation the remaining portion of the stomach had been anastomosed to the terminal portion of the ileum about 18 inches (46 cm.) above the ileocecal valve. There was no gastroileal ulcer. After disconnection of the anastomosis the opening in the ileum was closed, a small cuff of stomach was excised, and the gastric stump was joined to a proximal loop of jejunum in a posterior colic type of anastomosis. Recovery was uneventful. Serum protein measured 4.9 grams per 100 cubic centimeters of blood just before the patient's dismissal, and edema of the ankles was present.

In a letter 1 month after the patient's dismissal his daughter stated that he was doing well except for easy fatigue and no especial gain in weight. Diarrhea had not returned.

This was the only case in which previous partial gastrectomy had been performed.

The symptoms of gastroileal stoma are dependent chiefly on the location of the anastomosis and on whether or not ulceration is present.

Diarrhea was present in 6 of the 9 cases reported in this paper. In 5 of these it began immediately or within a few days after operation. In the 6th case a month elapsed before diarrhea appeared. The lienteric character of the stools was indistinguishable from that seen in cases of gastrojejunocolic fistula, but the latter would be unlikely as a cause of symptoms coming so soon after operation, a point which is of diagnostic value. Of the 3 other patients in the series 2 with upper ileal anastomoses had had vomiting. One interesting feature is that with but one exception (Case 2) diarrhea occurred only in those cases in which the anastomosis was very close to the large bowel. In 2 of the cases in which anastomosis was very close to the cecum, fecal belching occurred. Diarrhea coming quickly after operation is the chief reason for suspecting a gastroileal stoma. Epidemic diarrhea or postoperative ulcerative colitis might be confusing but cultures of stools and proctoscopic examinations help to distinguish these when seen early. Later these can be excluded rather accurately on the basis of the patient's history.

Vomiting may be of retention type and occasionally has a fecal quality or is accompanied by a belch with fecal odor.

Loss of weight may be severe and usually can be attributed to loss of partially digested food in the lienteric stools before adequate absorption occurs. Except for Case 5 significant loss of weight occurred in those cases in which there was diarrhea. This loss of weight probably would have been much more severe if there had not been some passage of food through the pylorus.

Pain in association with gastroileostomy may be of bowel type or of ulcer type. The former is usually lower abdominal and of cramping type with relief on passage of flatus, stool, or an enema. The pain of ulcer type may be burning or cramping and may be referred to the umbilical region or lower abdominal quadrants in much the same fashion as is the pain of gastrojejunal ulcer. Ulcer sequence and neutralization relief are atypical, however. When pain as a symptom is present the chances of finding a gastroileal ulcer or gastroileitis are good only when a significant amount of free hydrochloric acid is present on analysis of gastric contents. In 9 of the 10 cases thus far reported in which there was either gastroileal ulcer or gastroileitis, values of free hydrochloric acid obtained after Ewald test meals ranged from 30 to 74 units. In the other case analysis of gastric contents was not performed. In the 4 cases thus far reported in which there was free acid on analysis of gastric contents but no ulceration, the concentration was less than 30 units. Eight of the patients who had gastroileal ulcer were men, 1 was a woman, and the sex of the 1 remaining was not mentioned. All patients who had gastroileal ulcer had had peptic ulcer before operation.

Aside from the complications of gastroileitis and gastroileal ulcer, patients who have gastroileal stomas may be subject to nutritional deficiencies. In our series nutritional edema associated with hypoproteinemia, and multiple neuritis occurred. The external biliary fistula in Case 5 was apparently the result of an additional surgical error.

The diagnosis of gastroileostomy should be suspected if there is a history of onset of diarrhea very soon after gastroenterostomy. If the stools are lienteric and are accompanied by loss of weight, the possibility becomes strong. Vomiting and fecal belching may or may not be present. Roentgenological examination is of the greatest value in making the diagnosis.

If a gastroileal stoma is diagnosed and pain similar to that present with gastrojejunal ulcer exists, a gastroileal ulcer may be suspected. If the patient is a man, if he had an ulcer before his operation and now has free hydrochloric acid in greater concentration than 30 units after stimulation by a test meal, the chances are that either gastroileitis or frank gastroileal ulcer is present.

Treatment of gastroileostomy and gastroileal ulcer is surgical. The procedure used depends of course on satisfying the requirements of restoring adequate gastrointestinal continuity and of correcting the primary problem. Part of this may be accomplished by disconnection of the abnormal anastomosis and excision of any gastroileal ulcer. If the duodenum is normal nothing further may be required. If the duodenum shows evidence of healed or active ulceration, gastrojejunostomy may be sufficient. However, if either duodenal or gastroileal ulcers are active and secretion of free hydrochloric acid by the stomach is significant, it may be wise for the surgeon to consider partial gastrectomy. The prophylactic value of this procedure must be weighed against the additional risk imposed, especially if the patient's general condition has been depleted by the gastroileostomy.

SUMMARY

Gastroileostomy must be considered among the possible causes of symptoms occurring after gastroenterostomy. This type of anastomosis occurs as a surgical error. The cardinal symptoms of the gastroileostomy syndrome are diarrhea, vomiting, loss of weight, and pain. Diarrhea characteristically begins soon after operation and often is lienteric in type; vomiting occasionally has a fecal quality; loss of weight varies with the severity of diarrhea; pain is of bowel type when unmixed with that of gastroileitis or gastroileal ulcer.

Gastroileitis and gastroileal ulcers may simulate gastrojejunal ulcer clinically. They are present only when concentration of free acid is significant.

We have reported 8 cases of gastroileostomy and also 1 case previously reported but only recently confirmed surgically. Gastroileitis was present in 1 case and gastroileal ulcer in 3 cases in our series.

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PLASMA VITAMIN C AND PROTHROMBIN CONCENTRATION IN PREGNANCY AND IN THREATENED, SPONTANEOUS, AND HABITUAL ABORTION

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ANTEPARTUM bleeding occurs in early pregnancy with sufficient frequency to warrant consideration from every possible angle; Rutherford reported an incidence of 5 per cent in 1942. Of 24,289 pregnant women admitted to the Woman's Clinic of the New York Hospital, 9.0 per cent had vaginal bleeding, and of this number 1,648, or 1 in 15, suffered from a complete or incomplete abortion. Of the latter group, 59, or 3.6 per cent, were in the habitual abortion group, and were so designated because of 3 consecutive abortions, following the suggestion of Malpas. The incidence of habitual abortion was 1 in 411. The incidence of threatened abortion in this group of patients was 1 in 55. Therefore, antepartum bleeding in the first trimester of pregnancy is an important problem in itself, particularly so because of the unsatisfactory prognosis with regard to the associated pregnancy.

The underlying causes of the antepartum bleeding are manifold and are given in Table I. As can be seen, organic lesions, as well as other pathological states associated with gestation, require consideration in making a diagnosis of threatened or spontaneous abortion. Attention is directed to the large number of patients in the "undetermined" group. These causes, together with others, are illustrated in Figure 1.

Clinically, most abortions begin with painless bleeding in the second or third month of gestation, which time corresponds approximately to that when the placenta takes over the formation of progesterone. Seldom have the nutritional factors, which may play a rôle in the onset of such abnormal bleeding, been investigated. Evidence is slowly being accumulated which indicates that such bleeding at times may be due to a deficiency in vitamins C and K. It is our purpose to confine this discussion to these 2 vitamins and consider them, together with a nutritional program of adequacy, in the possible prevention of certain types of antepartum bleeding and, therefore, in the treatment of threatened, spontaneous, and habitual abortion.[1]

What rôle does a deficiency in vitamins C and K play in the production of the bleeding? A perusal of the literature reveals pertinent information. Mendive and Deulofeu have shown that the hypophysis, as well as the thymus, adrenal, spleen, testis, pancreas, and thyroid glands contained large amounts of vitamin C. Biskind and Glick have shown that the corpora lutea of cows contain abundant amounts of vitamin C and suggest a correlation with the production of progesterone. Israel and Meranze found a progesterone-like effect on the endometrium following the administration of ascorbic acid to infantile and ovariectomized rabbits. With regard to abortion, Voght observed that guinea pigs which had been given ascorbic acid frequently aborted. The clinical counterpart of this observation was provided by Ley who treated 10 cases of habitual abortion with success. The recent discovery of the antihemorrhagic vitamin K led Singleton to employ it clinically in the form of dehydrated young grasses in cases of abortion, with promising results. Javert found retroplacental hematoma and

TABLE I.—CAUSES OF BLEEDING IN THE FIRST TRIMESTER OF PREGNANCY, INDOOR SERVICE SEPTEMBER 1, 1932, TO DECEMBER 31, 1940

	Total cases
Abortion, complete or incomplete	1648
Threatened abortion	229
Undetermined	185
Ectopic pregnancy	85
Hydatidiform mole	33
Erosion or polyp	18
Myoma	5
Chorioepithelioma	4
Carcinoma of cervix	2
Total	2209

Total number of pregnancies studied 24,289
Incidence of bleeding in first trimester . . . . . 9.0 per cent

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[1]Presented at a meeting of the Dallas Southern Clinical Society on March 23, 1942, and at a meeting of the New York Academy of Medicine, April 29, 1942.

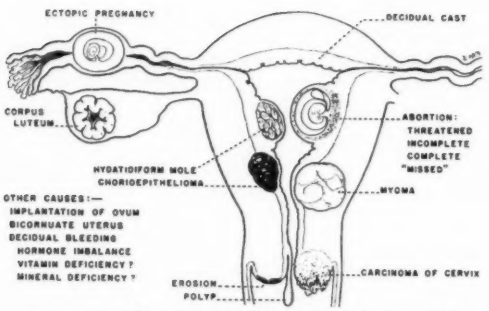

Fig. 1. Causes of antepartum bleeding in the first trimester of pregnancy.

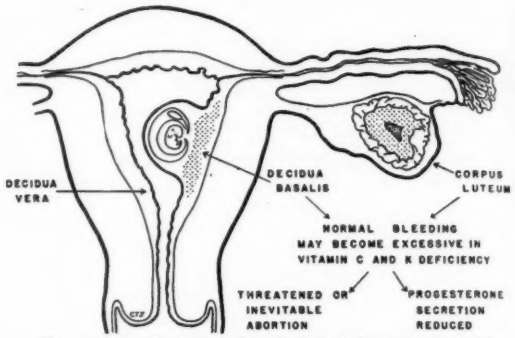
DECIDUA VERA
DECIDUA BASALIS
CORPUS LUTEUM
NORMAL BLEEDING MAY BECOME EXCESSIVE IN VITAMIN C AND K DEFICIENCY
THREATENED OR INEVITABLE ABORTION
PROGESTERONE SECRETION REDUCED

Fig. 2. Vitamin C and vitamin K deficiency as probable factors in the pathogenesis of spontaneous abortion.

hemorrhagic disease of the newborn in an infant with hypoprothrombinemia. An experimental study has been published recently by Moore, Bittinger, Miller, and Hellman, in which it was concluded that vitamin K deficiency and hypoprothrombinemia were factors in producing abortion in rabbits. Our own study provides a partial clinical application of their contention.

Theoretically, as indicated in Figure 2, deficiency in the antihemorrhagic vitamins C and K could cause excessive decidual bleeding, which Moore and his co-workers observed in hypoprothrombinopenic rabbits. If excessive, this deficiency could result in the death of the ovum, with expulsion 4 to 6 weeks later, or in the third month of gestation when abortion commonly occurs. At this period of gestation, the corpus luteum also increases rapidly in size, as Gillman and Stein have pointed out, and they regard the time between the 50th and 60th days as the critical period. If excessive bleeding occurs into the corpus luteum so that a corpus haemorrhagicum is produced, the production of progesterone may also be interfered with so that hormonal imbalance results, which provides a secondary or accessory factor in the pathogenesis of spontaneous abortion.

In this connection, the diet in pregnant women is very important. Williams and Fralin have shown that only 2 per cent of all women partake of an adequate diet in pregnancy. They observed vitamin deficiency in 50 per cent and mineral deficiency in 33 per cent. Teel and his co-workers have made similar observations. Ebbs, Tisdall, and Scott observed an increased incidence of abortion in patients having poor diets. In early pregnancy, morning sickness and vomiting may vitiate an adequate diet and thereby deplete the vitamin and mineral reserves.

PRESENT STUDY

PLASMA VITAMIN C IN NORMAL PREGNANCY

Digestion blood specimens were collected about 2 hours after breakfast from 246 patients at regular intervals during an uncomplicated gestation, at delivery, and in the puerperium, on the third day and 6 weeks postpartum. The patients were on the usual antepartum diet without vitamin supplement, and were either in the average or high economic status. Vitamin C was determined as ascorbic acid by the macrotechnique of Mindlin and Butler. A total of 376 specimens were examined, and the average values have been plotted in Figure 3. Twenty patients were studied separately at monthly intervals, but the concentration did not vary significantly from the average values. Many patients had 2 or more determinations on separate occasions.

The curve for vitamin C has a primary trend, which is downward from the average nonpregnant value of 1.1 milligrams per cent, as shown in Figure 3. The average total amount in the 376 specimens was 0.54 milligram per cent. This is only just above the level of 0.5 milligram below which patients are ordinarily regarded as deficient. The deficiency range was reached as early as the eighth week of gestation and was maintained throughout pregnancy. Individual variations were observed either above or below this concentration. The blood samples were digestion specimens, making this low range even more significant, for Todhunter and his associates have demonstrated that the ascorbic acid content of blood plasma begins to rise soon after the administration of 50 milligrams of vitamin C with the maximum rise in 1½ to 2½ hours. When the blood level was 0.5 milligram or less, the expected rise did not take place. Hydremia and maternal and fetal requirements may be factors in main-

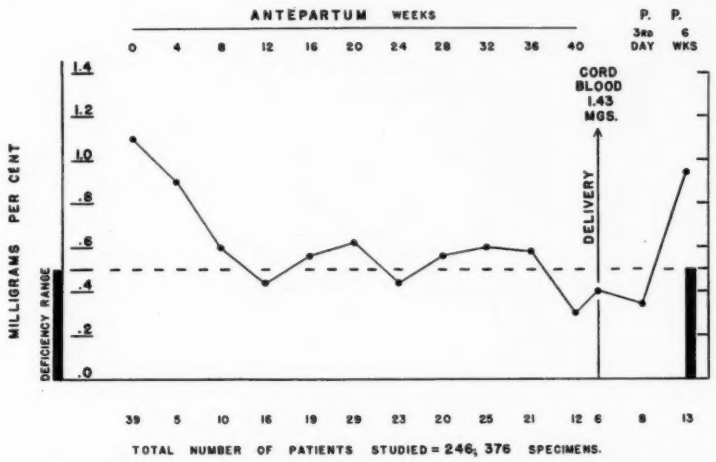

Fig. 3. Plasma vitamin C (ascorbic acid) saturation in normal pregnancy.

taining the low concentration in the second and third trimesters of pregnancy since they are also responsible for reduction in the cell volume and hemoglobin, as shown in Figure 5.

At term the maternal plasma contains about 0.4 milligram per cent of ascorbic acid. The values *at delivery* reported in the literature are at variance with each other. Abt, Farmer, and Epstein obtained an average value of 1.03 milligrams per cent, while Sadovsky and Wertheimer obtained a similar value, 1.09 milligrams per cent. Teel, Burke, and Draper reported a value of 0.52 milligram per cent which is more in accord with our own data. On the other hand, cord blood has a much higher concentration, 1.42 milligrams per cent, which compares favorably with the values reported by Teel, Burke, and Draper, Abt and his co-workers, and by Braestrup. It would appear that the maternal stores are depleted to supply the infant, and that the vitamin passes readily through the placenta.

The fetal requirements of vitamin C after birth are also of interest. During the first 10 days of life, there is a decrease from 1.07 milligrams to 0.27 milligrams according to Braestrup. Values ranging from 0.0 to 0.3 milligram were found in several of our infants who developed hemorrhagic disease of the newborn. The prothrombin concentration of these infants was probably very low. Perhaps a deficiency in vitamin C, in addition to hypoprothrombinemia, is necessary for the development of hemorrhagic disease. Javert has recently intimated that a lack of both vitamins C and K may be responsible for this disease in the newborn, since too many infants have hypoprothrombinemia without hemorrhagic manifestations. This view is borne out in part by the observations of Sanford and his co-workers, who found that infants with cerebral hemorrhage had low blood values for vitamin C.

On the third postpartum day, the blood vitamin C was 0.35 milligram, slightly lower than the value at delivery. The onset of lactation may be responsible for this low value, while wound healing (episiotomies and lacerations), and uterine involution and impaired intake must also be considered as contributory factors. During the first 14 days of lactation, Ingalls, Draper and Teel, and Sadovsky and Wertheimer found that breast milk contains from 4.5 to 4.62 milligrams of ascorbic acid per 100 cubic centimeters which is considerably higher than the amount present in the maternal plasma. At 6 weeks postpartum the vitamin C level had returned to normal, as indicated in Figure 3.

The daily oral administration of 100 milligrams of cevitamic acid and 100 cubic centimeters of orange juice to 100 deficient pregnant patients produced a rise in the plasma vitamin C to normal, showing that an adequate supplement will increase the content of this vitamin in the blood. This provides a clue as to the amount of vitamin C required to maintain normal concentration in the blood in pregnancy. Evidently about 200 milligrams is needed daily. Braestrup found that mothers on a deficient diet had vitamin C concentration of only 0.26 milligram per cent. This suggests that our deficient patients were also on

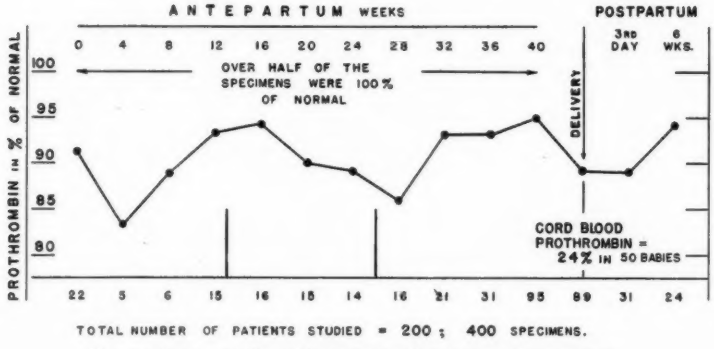
ANTEPARTUM WEEKS
POSTPARTUM
0 4 8 12 16 20 24 28 32 36 40
3RD DAY
6 WKS.
OVER HALF OF THE SPECIMENS WERE 100% OF NORMAL
DELIVERY
PROTHROMBIN IN % OF NORMAL
100
95
90
85
80
CORD BLOOD PROTHROMBIN = 24% IN 50 BABIES
22 5 6 15 16 15 14 16 21 31 95 89 31 24
TOTAL NUMBER OF PATIENTS STUDIED = 200; 400 SPECIMENS.

Fig. 4. Plasma prothrombin concentration in normal pregnancy.

inadequate diets despite the fact that their dietary history and economic level were considered satisfactory. Experience has indicated that diet and income do not always have a relation to the blood concentration of vitamin C in pregnancy. Food aberrations, nausea, and vomiting, common to parturient women, can vitiate the most adequate diet. Therefore, actual determination of vitamin concentration seems to be a better index of saturation or deficiency, in pregnancy, than the dietary history or the financial status of the patient.

PLASMA PROTHROMBIN IN NORMAL PREGNANCY

The plasma prothrombin concentration of 200 normal pregnant women has been discussed elsewhere by Javert and Macri, and the results are summarized in the curve in Figure 4. Studies of an additional 300 patients show no marked deviation from their original data. The curve has primary and secondary trends; the former is upward while the secondary trends vary with the trimesters of pregnancy. In the first trimester, the prothrombin concentration is lowest, probably due to a deficient intake of vitamin K, "morning sickness," or vomiting. However, the majority of patients (85 per cent) had an average prothrombin concentration ranging from 83 to 96 per cent of normal up to delivery. However, the average for the cord blood was only 24 per cent of normal.

Some of the patients with deficient values in vitamin C and prothrombin complained of bruising easily, epistaxis, bleeding gums, and vaginal bleeding. The latter was sometimes in the nature of a threatened abortion.

PLASMA VITAMIN C AND PROTHROMBIN DETERMINATIONS IN ABORTION PATIENTS

Plasma vitamin C and prothrombin determinations were made on 3 groups of patients; those having had either a threatened abortion, 1 or 2 previous spontaneous abortions, or habitual abortions (3 or more consecutively). Seventy-nine patients were studied. Data on these 3 groups of cases are given in Tables II and III. The total

TABLE II.—PLASMA VITAMIN C* (ASCORBIC ACID) IN PATIENTS WITH THREATENED, SPONTANEOUS, OR HABITUAL ABORTIONS

Group	Number of cases	Vitamin C in mgm. per cent		Deficiency 0.5 mgm. or less	
		Average	Range	Number	Percentage
Threatened abortion	20	0.46	0.08–0.81	14	70
Spontaneous abortion	37	0.30	0.00–0.98	27	73
Habitual abortion	22	0.36	0.10–0.98	14	64
Total	79	0.35	0.00–0.98	55	69
Control patients 4–16 weeks pregnant	50	0.55	0.00–1.6	25	50

*Mindlin and Butler macrotechnique.

TABLE III.—PLASMA PROTHROMBIN CONCENTRATION* IN PATIENTS WITH ABORTION

Group	Number of cases	Prothrombin concentration per cent of normal		Deficiency 70 per cent or less	
		Average	Range	Number	Percentage
Threatened abortion	20	65	22–100	13	65
Spontaneous abortion	37	46	23–100	30	81
Habitual abortion	22	61	15–100	14	68
Total	79	54	15–100	57	72
Control patients 4–16 weeks pregnant	60	92	70–100	9	15

*Warner, Brinkhous, and Smith technique.

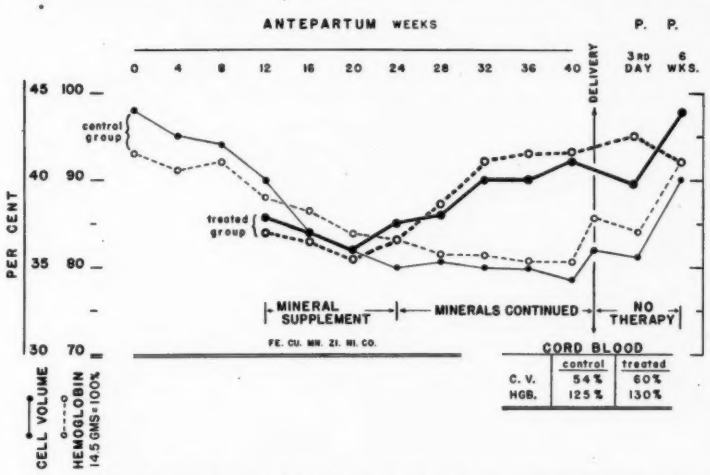

Fig. 5. Cell volume and hemoglobin determinations in normal pregnancy in a control group of 200 patients (1,000 determinations) and in a treated group of 8 habitual abortion patients receiving mineral supplement.

average value for vitamin C in all of the groups was 0.35 milligram per cent and was definitely lower than that found in normal pregnant patients used as controls. The incidence of vitamin C deficiency was 69 per cent in the abortion patients. The prothrombin concentration was studied in the same groups of abortion patients, and the values are presented in Table III. The average prothombin concentration was 54 per cent of normal, using the Warner, Brinkhous, and Smith technique. This is considerably below the normal value of 92 per cent observed in the normal control patients. The percentage incidence of prothrombin deficiency was 72 per cent in the abortion group. The relationship of prothrombin concentration to vitamin K (in the absence of liver disease) has been well established. It can be presumed that the abortion patients were deficient in vitamin K, since an elevation in the prothrombin level followed the administration of vitamin K to most of the patients having a low concentration.

Deficiency in both vitamin C and prothrombin (vitamin K) was present in 61 per cent of the patients. The remaining patients, 39 per cent, were low in either one or the other. Seldom did an abortion patient have normal values for both vitamin C and prothrombin. It would appear that deficiency in vitamins C and K plays an etiological rôle in the production of threatened and spontaneous abortion, as intimated above and shown in Figure 2. This deficiency may be the causative factor of the decidual bleeding which is often the first clinical sign of miscarriage. It seems significant that abortions occur most commonly in the second and third months of gestation when the vitamin C and vitamin K levels have been found to be low.

TREATMENT OF ABORTION

The results of clinical application of vitamin C and vitamin K therapy, together with a planned nutritional program of adequacy with regard to other vitamins as well as minerals, have shown considerable promise. In addition to an adequate dietary regimen, it has been our practice to use supplements of vitamin C in the form of fresh grapefruit, orange, lemon, or lime juice. Cevitamic acid, 100 milligrams daily, has been provided in addition when the blood values have been exceedingly low. Vitamin K has been supplied in watercress, spinach, cabbage, cauliflower, and dandelion greens. When the prothrombin concentration has been low, synthetic vitamin K has been given either orally as synkavite (Hoffman-LaRoche), 5 milligrams daily, or intramuscularly in amounts of 2 to 4 milligrams of thyloquinone (Squibb) in order to maintain a normal prothrombin level.

In addition to the above, a mineral supplement called endomin (Reed and Carnrick) has been employed to provide iron, copper, cobalt, nickel, and zinc. The endomin assisted in the prevention of a lowering of the maternal cell volume and hemoglobin that ordinarily is attributed to hydremia of pregnancy, as indicated in Figure 5.

TABLE IV.—FOLLOW-UP IN PATIENTS WITH THREATENED, PREVIOUS SPONTANEOUS, OR HABITUAL ABORTIONS

Group	Abortions in treated group			Abortions in untreated group			Grand total
	Total number	Number	Percentage	Total number	Number	Percentage	
Threatened abortion	10	2*	20	10	10	100	20
Previous spontaneous abortion	9	0	0	28	28	100	37
Habitual abortion	14	1	7	8	8	100	22
Total	33	3	9	46	46	100	79

*1 hydatidiform mole.

Moreover, manganese plays a part in the maintenance of normal gestation according to Everson and Daniels, who found that stillbirths increased in mice when this mineral was omitted from the diet. Iron has been used in the form of perchloride in the treatment of recurrent abortion, according to Malpas. Simmonds has called attention to the relation of vitamin E to iron metabolism. While no tests for vitamin E were employed, it was assumed that when the prothrombin and vitamin A values were low, a deficiency of vitamin E probably also existed, since it is also a fat soluble vitamin. Therefore, vitamin E in the form of alphatochopherol (Squibb) was given intramuscularly, 240 milligrams monthly, to some of the patients, while others received wheat germ oil, or tochophorex (Squibb) orally. It seems more than probable that there is an interrelationship of many minerals and vitamins for the maintenance of nutrition, as is well illustrated by the relation of calcium and vitamin D.

Hormonal therapy was incorporated into the regimen as indicated. The dosage of progesterone was 1 milligram weekly in the first weeks of pregnancy, or when abortion threatened. A few patients received no progesterone. Some of the patients had a low basal metabolic rate, and these women were placed on thyroid extract, .015 gram 3 times daily. This medication is seldom continued beyond the fifth month when the metabolic rate begins to increase normally.

Constipation is undesirable. Mineral oil and olive oil were interdicted because their use has been found to be associated with hypoprothrombinemia in a large number of patients. Saline catharsis or enemas are preferred.

A defect in the zygote has been found by Irving and Streeter to be the cause for abortion. Since patients with repeated abortions often present no sterility problem, it may be assumed that in many instances the ova and sperm are normal. Several husbands had normal semen specimens. In the cases of women with threatened abortion, Kotz and his co-workers found that only 4.9 per cent of the infants carried to viability had congenital abnormalities. In our own clinic, 2.95 per cent of 27,000 infants delivered had some abnormality, including extra digits, birth marks, undescended testicles, umbilical hernia, spina bifida, and hydrocephalus. It would appear, as our experience to date indicates, that infants born to mothers with threatened or repeated abortion are not necessarily malformed, although the tendency may be greater.

The results of the nutritional regimen in the treatment of threatened, spontaneous, and habitual abortion, as here outlined, are shown in Tables IV and V. The percentage of abortions in the threatened group is 20 per cent and it is considerably lower in the control group. No abortions occurred in the group of women with 1 or 2 previous abortions even though one could expect that 22 and 38 per cent, respectively, would abort, according to Malpas. The incidence in the habitual abortion group was only 7 per cent, which is much lower than the incidence of 73 to 94 per cent reported by Malpas. The total incidence of abortion in the 3 groups of patients is also decidedly lower than the incidence of 100 per cent in each of the untreated control groups.

The percentage of live births in the threatened abortion group is 100 per cent, whereas Ruther-

TABLE V.—LIVE BIRTHS IN TREATED PATIENTS WITH THREATENED, PREVIOUS SPONTANEOUS, OR HABITUAL ABORTIONS

Group	Number delivered cases	Live births		Undelivered
		Number	Per cent	
Threatened abortion	4	4	100	4
Previous spontaneous abortions	9	9	100	3
Habitual abortion	12*	11	91	1
Total	25	24	96	8

*1 erythroblastosis fetalis.

ford found that only 24 per cent of such fetuses reached viability. The group of women with 1 or 2 previous spontaneous abortions also had an incidence of live births of 100 per cent. In the habitual abortion group 91 per cent of the women had live births. However, in this type of patient, MacGregor and Stewart reported a 10 to 20 per cent chance of a successful pregnancy. The percentage of live births ordinarily ranges from 85 to 89 per cent of living fetuses so that the results (96 per cent live births) is impressive. However, the number of delivered infants is small, so that this phase of the problem must be regarded as beyond the scope of this paper which deals primarily with the prevention and treatment of abortion.

SUMMARY

Intelligent treatment of antepartum bleeding in the first trimester of pregnancy requires an accurate knowledge of the underlying causes. An adequate diet is essential in the prevention of abortion. Evidence is being accumulated to indicate that vitamins C and K and the mineral supply of the mother may be vital factors in the early growth of the embryo. Supplementary administration of certain vitamins and minerals is advisable when laboratory tests indicate a deficiency. Endocrine therapy may prove of value in selected cases. Thyroid extract is indicated when the basal metabolic rate is low, especially if, under such circumstances, vitamin and mineral supplements are employed.

Since the causes of abortion are numerous, any method of treatment will result in some failures. At times, an Aschheim-Zondek test may be necessary to determine whether treatment should be continued.

With the above possibilities in mind, a series of 79 patients with threatened, spontaneous, or habitual abortion were treated with a nutritional program of adequacy. The incidence of abortion in these 3 groups of patients was 20, 0, and 7 per cent, respectively, whereas it was 100 per cent in each of the control groups. Live births were obtained in 96 per cent of the total number of patients that have delivered, as shown in Table V.

CONCLUSIONS

1. Antepartum bleeding in the first trimester of pregnancy occurred in 9.0 per cent of 24,289 patients, and was most frequently associated with the abortion state.

2. Evidence is being accumulated showing that the antihemorrhagic vitamins C and K may be factors in the pathogenesis of certain cases of threatened and spontaneous abortion.

3. Plasma vitamin C decreases in normal pregnancy from nonpregnant values of 1.1 milligrams per cent to 0.35 or 0.4 milligram per cent at term. There is little reduction in the plasma prothrombin concentration during pregnancy. Dietary aberrations, nausea and emesis, hydremia, and maternal and fetal requirements may lessen the value of a diet that is adequate. Deficiency in vitamins C and K can be prevented by administering cevitamic acid and synthetic vitamin K.

4. The cord blood contains several times the amount of vitamin C found in maternal plasma at delivery, showing that this vitamin easily traverses the placenta. However, prothrombin does not, and even though it has been demonstrated that vitamin K passes the placental barrier, the fetal prothrombin level is ordinarily about one-third of the maternal level.

5. Several infants with cord blood values of 0.0 and 0.3 milligram for vitamin C developed hemorrhagic disease of the newborn. Since hypoprothrombinemia is almost universal at birth, whereas the vitamin C level is usually satisfactory, it is probable that hypovitaminosis of both vitamins C and K are necessary for the development of hemorrhagic diathesis and that deficiency in only one may fail to produce abnormal bleeding.

6. Of 79 patients with threatened, spontaneous, or habitual abortion, deficiency in vitamin C was found in 69 per cent, and deficiency in prothrombin (vitamin K) was present in 72 per cent. Hypovitaminosis of both vitamins C and K was present in 61 per cent of the patients. These patients usually complained of skin ecchymoses, epistaxis, bleeding gums, and vaginal bleeding.

7. Deficiency in vitamins C and K, individually or together, may play an etiological rôle in the production of some cases of antepartum bleeding and abortion.

8. A nutritional program of adequacy with regard to vitamins C and K; minerals, especially iron and manganese; and hormones such as thyroid and progesterone appear to be effective in certain cases in the prevention of antepartum bleeding and abortion.

9. A clinical study of 33 adequately treated patients with either threatened abortion, 1 or 2 previous abortions, or 3 or more consecutive (habitual) abortions showed that the abortion incidence was 20, 0, and 7 per cent for each group respectively, whereas, in each of the control groups having a total of 46 patients, the abortion rate was 100 per cent. Twenty-five of these patients have delivered 24 living infants, or 96 per cent have had live births.

10. More investigation is necessary before one can state which vitamin, hormone, or mineral is solely responsible. However, the treatment of choice seems to be a combination of these factors beginning before conception and continuing during pregnancy.

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ACUTE HEMATOGENOUS OSTEOMYELITIS JUVENALIS

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ALTHOUGH the incidence of acute osteomyelitis has varied little during the past few years, its surgical management has definitely changed from a radical to a more conservative regimen. This has resulted chiefly from the discovery of the sulfonamide drugs, the production of a potent high titer staphylococcal antitoxin, and the rediscovery of an old surgical principle (immobilization) concerning infected tissues. Acute ostomyelitis, regardless of its varied clinical manifestations, has always been considered a single clinical entity and treated accordingly. Consequently, the mortality and morbidity have been high and these will not be reduced until the clinical variations of this disease are appreciated. Only when we realize that acute osteomyelitis is due to the Staphylococcus aureus in over 83 per cent of the cases, and that not the bacteria, but their toxins are responsible for the systemic reaction and local destruction of osseous tissue, can we intelligently treat the disease and obtain complete recovery, with minimal bone destruction.

There are over 60 varieties of staphylococcus and according to Spink, no less than 8 different types of toxins are derived from these. Each type of toxin has a definite specific reaction on the tissues in which it has been generated (local reaction) as well as on the generalized somatic cells and glands (systemic reaction). These toxins, reacting in the tissues, destroy both the fixed and mobile tissue cells. The most powerful of these toxins will kill a person within 15 to 36 hours, as demonstrated in the Queensland cases. Twelve children who received diphtheria toxin succumbed within 15 to 36 hours. Deaths were due to contamination of the diphtheria culture in obtaining the toxoid from lethal toxins of the Staphylococcus aureus.

The necrogenic toxin and the toxin that increases diffusibility of both the bacteria and their toxins in the tissue cause extensive destruction of the osseous tissue. The hemolytic, leucocidin, and fibrolysin toxins together with the power of diffusibility are responsible for the failure of localization of the infection. Therefore, the early high mortality in acute osteomyelitis is caused from the profound toxemia with or without bacteriemia. The bacteriemia in all probability is due to a bacterial thrombophlebitis in the osseous tissue. The number of colonies in the circulating blood is entirely dependent upon the degree and extent of the thrombophlebitis which in turn is determined by the virulence of the organism, both being secondary to the type of toxin liberated. That thrombophlebitis exists in all pyogenic infections is a well established pathological law. However, the extent and size of the veins involved are dependent upon the type of toxin liberated by the staphylococcus and vary considerably in degree. Therefore, it is readily understandable that early neutralization of the toxin not only will inhibit all the side effects of the infection, such as extensive injury to the somatic tissues including all organs and glands, but will prevent local osseous tissue destruction as well. If this can be accomplished, then the somatic tissue cells, especially the reticuloendothelial system, can destroy the bacteria both by phagocytosis and the liberation of bacteriolysins and agglutinins. The sulfonamides are a valuable adjunct because they inhibit bacterial growth and thus prevent toxin liberation.

Acute osteomyelitis can be divided into several clinical types depending entirely upon the kind of organism and its toxin. In teaching, I have classified acute osteomyelitis clinically to correspond with the pathological physiology. (1) Profound systemic effects with minimal local reaction is due to the lethal or sublethal toxin liberated by the staphylococcus. Bacteriemia may or may not be present. Blood culture is, however, positive in a high percentage of these cases. (2) Profound systemic as well as local reaction is caused by liberation of the lethal or sublethal toxin and is accompanied by early cellulitis resulting in pus formation with or without associated bacteriemia. (3) Minimal systemic and maximal local reaction without bacteriemia is probably the result of the necrogenic toxin and the spreading factor of "Duran-Reynolds." Pus forms rather early in the majority of cases. (4) Minimal systemic and local reaction is rare and frequently leads to Brodie's abscess. Here virulence of both the staphylococcus and its toxin is of a mild character. (5) The streptococcal form, occurring in young children and babies, usually causes minimal bone destruction. (6) In the chronic forms, such as Brodie's abscess and chronic sclerosing osteomyelitis of Garre, the systemic and local reactions are nil.

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Infection within osseous tissue varies greatly depending upon the degree of bone involvement. In some, early localization occurs, whereas in others, there is present a diffuse marrow and haversian cellulitis which localizes to one area in the bone or fails to localize, resulting in a diffuse cellulitis of the entire shaft of the bone. If the infection begins near the cortex in the metaphysis and localizes early, it ruptures and a subperiosteal abscess forms. If the infection begins in the metaphysis near its center close to the beginning of the bone marrow, a diffuse cellulitis of the bone marrow appears. This form of infection is comparable to the cellulitis of soft tissue. In lymphangitis and cellulitis if the infection localizes, a simple abscess appears; if not, the whole cellular structure of a part becomes involved and frequently death occurs. It is this diffuse osseous and bone marrow cellulitis and lymphangitis which is responsible for the profound systemic reaction so frequently encountered in acute osteomyelitis. Therefore, the anatomical location of the primary infection within the metaphysis has a direct bearing upon the type and extent of the osseous lesion. Thus, the pathological condition of the bone can be classified as follows: (1) Diffuse cellulitis involving the entire shaft, (2) diffuse cellulitis involving the entire shaft with localization to one or more areas, resulting in multiple abscesses or a single abscess. Occasionally, in this type, an abscess is centrally located at each end of the shaft. (3) Superficially located primary focus with early subperiosteal rupture and abscess formation which frequently ruptures into the soft tissue. In these cases a minimal amount of bone is destroyed. (4) Primary focus located near the epiphysis in the center of the metaphysis, resulting in a centrally located abscess. Often the joints are involved in the two latter. A careful evaluation of both systemic and local reactions will indicate the pathological condition which is present or which will develop in the osseous tissue.

Based on the pathological condition, the treatment is simple and the results, in the majority of instances, will be most gratifying. Treatment consists of complete rest; early neutralization of the toxemia; early prevention of bacterial growth; maintenance of water balance, blood volume, plasma volume, blood cellular volume and blood electrolytes; complete immobilization of the involved part; daily blood cultures in all cases; maintenance of nutrition; and finally, operation only when cellulitis has localized with abscess formation.

Early neutralization of the toxin and prevention of bacterial growth will immediately overcome the toxemia, thus prevent bone destruction, and probably obviate the necessity of operation in a large number of cases. This purpose can be accomplished by the daily administration of 60,000 to 100,000 units of a potent antistaphylococcal serum until toxemia subsides. The intravenous or oral administration of sulfathiazole prevents the multiplication of bacteria and, consequently, the formation of toxin by bacteriostatic action. This allows the reticuloendothelial system to manufacture bacteriolysin and agglutinins as well as phagocytes which eliminate the infection. Early immobilization will minimize or prevent the spread of infection, especially to the joints. The only other treatment is supportive, i. e., injections of glucose in Ringer's solution and plasma and whole blood transfusions. This therapy must be continued until the patient can supplement intravenous medication by ingesting the necessary food. Large doses of vitamins, especially B_1 and C, should be given intravenously during the toxic phase and later by mouth. Vitamin C changes precollagen to collagen fibers. Vitamin B_1 is essential for the normal function of the nervous system and should be given in 10 to 20 milligram doses. Vitamin D and calcium should be given after the toxemia subsides.

Frequent radiographic studies and needling for pus after the toxic stage should not be forgotten. If the roentgenograms demonstrate bone necrosis and the temperature returns to normal, operation should be deferred and frequently will not be necessary. However, if pus is obtained, operation under local anesthesia is indicated. If there has been local central bone destruction and the toxemia has subsided, but the patient continues to have fever, operation is indicated if it is cautiously undertaken. If the patient can be treated within 24 hours of onset of the disease according to this plan, bone destruction will be minimal.

Any surgical procedure undertaken during the acute stage will result in a high mortality and morbidity with serious disability. Although operation is contraindicated in the majority of other infections with profound toxemia and bacteriemia, some surgeons insist on using the drill and chisel in similar cases of osteomyelitis. Butler reported 123 cases of acute osteomyelitis with a positive blood culture in which early operation was performed with a mortality of 52 per cent; whereas in 122 cases with negative blood cultures, early operation resulted in only a 2 per cent mortality. Neither staphylococcal antitoxin nor sulfonamides were used. These statistics emphasize the importance of instituting proper treatment early in acute hematogenous osteomyelitis.

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MODERN METHODS IN ANESTHESIA AND THE WAR

LACK of experience of a situation sometimes leads to ill founded conclusions. It is probable that neither the care of accidents in civil practice nor the performance of necessary surgical procedures for soldiers and sailors in time of peace have constituted an adequate background of experience from which to predetermine our conduct under the circumstances of war. Doubtless both surgeon and anesthetist will modify their plans of action as experience with battle casualties becomes extensive in the months and years to come. It would seem advisable, therefore, to emphasize principles rather than minutiae of practice in our preparation for the duties which confront us.

There is a variety of anesthetic agents available for the relief of pain. Several techniques for the administration of these drugs have been used in civil practice. On superficial consideration, it might be concluded in the interest of simplicity that one or two drugs given by one or two techniques should be chosen for military practice. However, further reflection brings out many objections to such a conclusion. For instance, it may be assumed that the variety and gravity of disturbances of the physiological functions of the respiratory and circulatory systems which are encountered among the wounded will be as great as, if not greater than, the variety of such disturbances common in civil practice. Hence, the demand for a varied attack by the military anesthetist may be even greater than in civil practice. A physician trained in anesthesiology may contribute many services in addition to the prevention of pain due to operations. The management of fluid depletion, transfusion and other intravenous therapy, inhalation therapy, the maintenance of free breathing under all circumstances, the use of manual and mechanical aids to respiratory exchange and the judicious relief of pain before and after operation or for nonsurgical cases are some of the fields in which comprehensive knowledge and experience in anesthesiology may be helpful. Emphasis upon principles and a broad consideration of techniques in our preparation for war has therefore seemed wise. The Offices of the Surgeons General have very laudably instituted certain changes of a promising nature. Whether or not Tables of Organization have yet been revised to recognize fully the needs of anesthesia, there has been an encouraging assignment of qualified anesthetists to each hospital if not to each surgical team. Medical officers on active duty are being instructed in anesthesiology in civilian as well as military hospitals.

As the number of anesthetists available in the medical corps increases, the care with

which they are assigned to duty becomes important. The director of anesthesia in a large hospital ought to be an officer with broad experience in a similar position in civil life. If the scarcity of men with such experience makes it necessary to assign officers trained during the present emergency to positions of such responsibility, due consideration ought to be given to previous executive experience in other fields. As soon as the number of well qualified officers is sufficient, it should be recognized that one anesthetist may be assigned with advantage to every surgical team. Particularly is this true of units dealing with chest and abdominal wounds. How extensively technician aids (hospital corps men or nurses) can be utilized safely, will depend upon the caliber of instruction and supervision which the officer in charge of anesthesia is capable of giving.

The type of apparatus provided for the anesthetist in our armed forces is of some importance. The proper "tools" of any "trade" come into existence in response to evident need as a result of long experience. It is obvious that present lists in tables of supplies of the military organizations have had to be made up without observation of the needs, and with very little experience in anesthesia under war conditions. An honest effort to provide the best equipment on the market has evidently been made. Certainly no expense has been spared. News from anesthetists in active service indicates that certain of the simpler but more essential and less expensive pieces of equipment are not available. For instance, a simple assembly of a face mask, strong rubber breathing bag, and proper artificial airways with, or even without, a cylinder of oxygen constitutes a very efficient aid for resuscitation. With these articles available, respiratory obstruction, depression, or arrest may be quickly and satisfactorily treated. In addition, a simple folding type of anesthetist's laryngoscope with two or three artificial breathing tubes, and a small suction catheter to pass through such tubes into the bronchi, puts the officer in command of the situation even when the lower respiratory tract is contaminated by blood or other fluid. If a properly shaped canister of soda lime granules is available to insert between the mask and breathing bag mentioned as useful for artificial respiration, an efficient apparatus is provided for the administration of ether (or the gaseous agents). A small supply of oxygen is necessary under such circumstances. Thus equipped, an officer familiar with modern practice in anesthesia can administer atmospheres under positive pressure, a procedure sometimes helpful in the treatment of chest injuries, and for anesthesia during operations within the chest. The bulk, cost and efficiency of simple equipment of the sort just mentioned would seem particularly well adapted to military needs. By competent officers, it might even be used under field conditions.

Medical officers, whether serving on land or sea, not infrequently find themselves under the necessity of being "all things to all men." Knowledge or skill in only one specialty cannot avail at such times. Common sense is the best substitute for deficiency of either knowledge or skill. It must be admitted, however, that among the more frequent disabilities encountered will be acute interference with the normal functions of respiration and circulation. Major injuries to the upper and lower respiratory tract, loss of blood, and severe pain are common results of battle. The anesthetized patient during operation provides ideal material with which the teacher may demonstrate and the officer may practice the care of respiratory and circulatory emergencies. Protection of respiratory and circula-

tory function is the essence of good anesthesia. The "bad results" of anesthesia are, in no small measure, due to neglect of such protection. It seems obvious, therefore, that knowledge of anesthesiology, skill in the replacement of fluids, in the insertion of artificial airways, in safe and efficient methods of artificial respiration, in clearing the respiratory tract of blood or fluid, together with skill in relieving pain will be found useful wherever the medical officer's duties may take him. The courses in anesthesiology sponsored by the War Department are designed to provide instruction along these lines.

Fear has been expressed that short term instruction in the surgical specialties now sponsored by the War Department may result in a surplus of poorly trained specialists coming back to civilian practice after the war. Such a condition is not likely to arise in the field of anesthesiology. It is important to remember the definite shortage of clinical anesthetists which existed prior to this war. Those officers receiving instruction and experience during the war will be in a position to render better service than formerly to their patients when they return to civil practice, regardless of whether or not they choose anesthesia as their special field.

The Surgeons General of the Army and of the Navy are to be congratulated upon their efforts to provide modern anesthesia, as well as modern medical service of every sort, to the armed forces. It seems probable that the results will justify this attitude.

RALPH M. WATERS.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IN any small book as *Acute Injuries of the Head*[1] by Rowbotham (287 pages), the author invariably faces a serious criticism when he attempts to cover such a large subject as acute injuries of the head in such a limited space. He runs the risk of being accused of knowing or of believing and practicing no more than he has actually written, though obviously in most cases this fact must not be true. As he indicates in his preface, Rowbotham is aware of this possibility.

In order to cover the subject completely the author has not deviated from his outline of discussion; the book is absolutely lacking in any digression or padding. In fact, this is so much true that one frequently finds broad and arbitrary statements which need explanation and elaboration. The treatment of diagnostic signs and symptoms is clear and concise, with sufficient detail, and the short descriptions of the gross brain pathology are excellent. The author's use of drugs in the treatment of acute cerebral injury will be questioned by many surgeons, but no one will take objection to his views on the importance of local anesthesia in this type of surgery. On page 181, the statements referable to the use of amniotic membrane in the repair of cerebral trauma should never be found in a text printed as late as the spring of 1942. The author seems to find indications for operation in acute cerebral trauma much more frequently than does the average American neurological surgeon, and he has stated clearly his indications for subtemporal decompression when intracranial tension is greatly increased due to swelling of the brain. Such an operation is indicated when there is: (1) retrogression following a period of improvement which cannot be controlled by spinal drainage or by intravenous hydration; (2) a delayed decerebrate rigidity; (3) a fixed dilated pupil; or (4) prolonged unconsciousness associated with persistently high cerebrospinal fluid pressure. The uninitiated would not learn from the discussion on the operative treatment of increased intracranial tension and cerebral herniations just what insurmountable difficulties and real trouble can be created by surgery of such a nature.

There is a brief but useful and unconventional discussion of the postconcussional syndrome and some useful notes on the medicolegal aspects of cerebral injuries and surgery. The illustrations, though not plentiful, serve their purpose splendidly. The greatest criticism of the book lies in some of the dogmatic principles of treatment, especially those relative to surgical treatment, and though such methods no doubt have served well in the hands of Rowbotham, by no means are most such principles in common use in America. Appearing at this time, when the cerebral injuries of warfare are increasing steadily, it will be most interesting, five years or so hence, to reread this pithy book in the light of our then newly acquired experience.

JOHN MARTIN.

[1] ACUTE INJURIES OF THE HEAD; THEIR DIAGNOSIS, TREATMENT, COMPLICATIONS, AND SEQUELS. By G. F. Rowbotham, B.Sc. (Manch.), F.R.C.S. (Eng.), with a foreword by Norman M. Dott, M.B., Ch. B. (Ed.), F.R.C.S. (Ed.). Baltimore: The Williams & Wilkins Co., 1942.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

SAFE DELIVERANCE. By Frederick C. Irving, M.D. Boston: Houghton Mifflin Co., 1942.

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